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BULLETIN

OF

THE NEW YORK ACADEMY OF MEDICINE

JUNE, 1931

INCORPORATED 1851

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ANNUAL GRADUATE FORTNIGHT

SERUM THERAPY*

WILLIAM H. PARK

Director of Laboratories, Department of Health

We have just heard the paper by Dr. Zinsser taking up from a research point of view the nature of antibodies. I have been asked to consider antibodies from another standpoint, by giving a short paper on the utilization of antibodies in the treatment of communicable diseases. As he has already told you, antibodies divide themselves into two distinct classes, the antitoxic and the antibacterial antibodies. Most of the diseases in which we use antibodies for curative purposes are either due to bacteria causing definite extracellular toxins or to those in which the injury seems to be due chiefly to the bacterial substance. It is possible that undetermined intracellular toxins may play a more or less important part in some of them. The hemolytic streptococci, exciting scarlet fever, erysipelas, puerperal fever, septic sore throat and possibly other infections produce poisoning through exotoxins and endotoxins.

The antitoxic sera are more potent than the antibacterial sera, and when we treat cases having diphtheria and tetanus, there is no difficulty in giving sufficient antitoxin to be effective if we reach the cases early enough.

* Delivered October 29, 1930.

With the antibacterial sera we have to utilize the body fluids and cellular elements to aid the antibodies of the antiserum to destroy the microörganisms and this limits the effective treatment of the cases.

The first disease I shall touch upon is: *Diphtheria.* There is probably little new that I can say to you on the use of antitoxin in this disease. In a case of diphtheria we know that the toxin is situated in the region of the upper respiratory tract which is attacked, and that the toxin unites first with the adjacent tissue and then the excess passes by the lymphatic channels to the blood and so is distributed throughout the body. We know from experimental investigation, that there is a period of a few hours after the toxin has come in contact with the cells that the union is incomplete and that the toxin can still be neutralized by the antitoxin. When, however, union has taken place, little or no good results from the use of antitoxin. If for instance, we give a rabbit an intravenous injection of ten fatal doses of diphtheria toxin, we cannot neutralize that toxin if we delay the giving of antitoxin for more than one and a half hours. Fortunately in an ordinary case of diphtheria a very moderate amount of toxin escapes being fixed by the local tissues and passes to the blood within the first 24 hours. In considering the dosage of antitoxin we must keep in mind that it is not the amount of toxin in the body which determines the amount of antitoxin to be given. If all the toxin in the most malignant case could be extracted and placed in contact with antitoxin less than 100 units of antitoxin would neutralize it. We give much larger doses than this because the antitoxin after entering the blood gradually passes through the walls of the capillaries to be dispersed to all regions of the body. As only a slight percentage of the antitoxin in the blood passes out through the capillaries within a limited period of time, we realize the wisdom of giving a great excess, so that in a short time the amount which passes to the tissues will be sufficient to neutralize any unattached toxin. The need of speed in severe cases makes us choose different

methods for administering antitoxin in mild, moderate and severe cases. In mild cases an intramuscular or even a subcutaneous injection of a moderate amount is good treatment, in severe cases an intravenous combined with intramuscular injection is much more effective. In very severe and toxic cases an intravenous injection is absolutely indicated. The serum when given should be fairly warm.

The objection to the intravenous injection is that there is a slightly greater danger of severe shock, perhaps even fatal anaphylactic shock. This occurs possibly once in 20,000 cases, while in intramuscular injections, probably only once in 60,000. If, however, we inquire as to the history of asthma and as to whether previous injections of horse serum have been given, and neither of them is true and if we also give the serum very slowly, there is almost no chance of serious consequences. Even if a history of asthma or previous serum injections is obtained, it is probably wise, in a severe case to give an intravenous injection, but it should be done very slowly. We may possibly at some time cause a death by giving it intravenously in these cases, but meanwhile we will have saved many who would otherwise die. In the following table is given our present practice.

AMOUNT OF ANTITOXIN REQUIRED IN THE TREATMENT OF A CASE

	Mild Cases	*Moderate*	**Severe*	**Malignant*
Children up to 60 lbs. in weight (under 15 years of age)	3,000 units to 5,000 units	5,000 units to 10,000 units	10,000 units to 20,000 units	15,000 units to 30,000 units
Older children and adults 60 lbs. and over in weight	3,000 units to 5,000 units	10,000 units to 15,000 units	20,000 units to 40,000 units	30,000 units to 60,000 units

Cases of laryngeal diphtheria, moderate cases seen late at the time of the first injection, and cases of diphtheria occurring as a complication of the exanthemata should be classified and treated as "severe" cases.

In all cases a single dose of the proper amount, as indicated in the schedule, is recommended. No further injections of antitoxin are necessary.

It is recommended that the methods of administration be as follows:

Mild Cases—Intramuscular.

Moderate Cases—Intramuscular.

Severe Cases—Intravenous or partially intramuscular.

Malignant Cases—Intravenous.

*When given intravenously the smaller amounts stated.

There is still doubt in the minds of many physicians whether a single dose of antitoxin is sufficient. There is no question that usually twelve hours after the first injection of antitoxin, many cases still remain very sick and that if a second dose is given, they may in the next 12 hours become much better. If, however, one does not give the second injection, one will just as often find them improved. It takes a certain length of time for the antitoxin to neutralize the toxin in the tissues and for the inflammatory reaction to begin to subside. Some probably do not fully appreciate the fact that the antitoxin in an intramuscular injection is only gradually passed out to the blood. At the end of 24 hours only about sixty per cent has been absorbed, and it is two days before it is almost entirely absorbed. It is as if repeated tiny injections were being given intravenously every half hour for two days. There is no harm in repeating the injections, but if a sufficient dose has been given at the first injection, there is no advantage, while there is distinct harm in giving half the amount needed at the first injection and supplementing this with a second dose twelve hours later.

One can usually detect those in whom injection of serum will be followed by the development of untoward symptoms by finding out whether the mucous membrane of the eyelid reacts to serum. We place a drop of the serum on the eyelid and wait for 15 minutes. If no reaction develops, there is little probability of its following a dose of serum. If a reaction does develop we use great caution in giving a therapeutic dose.

The question as to how much we can desensitize a patient is still debatable. If 5 c.c. of serum are given subcutaneously or intramuscularly and no reaction results, we are almost certain that no reaction will develop if we repeat the dose. If we double it, however, we may get a reaction. There is some degree of desensitization, but it is not at all something which can be relied upon. The dosage of antitoxin varies between the following limits.

The use of antitoxin to produce passive immunization against diphtheria is exceedingly successful. I doubt whether any case of diphtheria has ever developed within a week after a person had received a thousand units of antitoxin. We must remember that this passive immunity is not lasting. It is quite different from that which develops after toxin-antitoxin or toxoid. It is interesting to note that in the 35 years which have elapsed since the discovery of antitoxin and the twelve years since the general use of toxin-antitoxin or toxoid, that the death rate has been reduced from 150 to about 3.

Undoubtedly, the severity and mortality of diphtheria have lessened considerably during these 35 years owing to general health measures, but the most careful scrutiny of the facts makes us confident that much of it is due to diphtheria antitoxin and to toxin-antitoxin.

This is the next disease that I wish to discuss. *Tetanus*:—Every clinical case of tetanus is a late one. There is in the infected wound no suggestion of tetanus infection. It is only when the nervous and muscular systems have become involved that we realize that tetanus toxin has been acting for some time. There are only two proper methods of administering antitoxin in tetanus. One is through intravenous injections, the other through intraspinal injections. These two methods should be combined. Experimental evidence shows us that an animal can be saved by an intraspinal injection when it cannot be saved by an intravenous injection and the majority of those who have had most to do with the treatment of tetanus, believe that there is convincing evidence that the same is true for the treatment of human beings. We have just stated that in diphtheria we give only one dose of antitoxin. In tetanus, we give several doses. We have some evidence that it is advisable to keep the antitoxic content of the spinal fluid and of the blood at a high level. It is possible that the first injection of the antitoxin both intraspinally and intravenously accomplishes nearly all the good that successive treatments accomplish. However, the disease is such a

dreadful one that we want to do everything that seems to be of possible avail. We must remember that in the severe and rapidly advancing cases, antitoxin will probably be given too late to do any good. It is in the moderate cases which would probably be fatal without treatment that antitoxin shows its best effect. Generally we begin then by giving an intraspinal injection of 10,000 to 15,000 units and an intravenous injection of the larger amount. In twelve hours we give another intravenous injection and in 24 hours a second intraspinal injection. If the case does not seem greatly improved, we continue an intraspinal injection every day for two or three days. After ceasing to give intraspinal injections we give a dose of antitoxin intramuscularly every two or three days until the case has recovered or died. It is probable that any case that receives 100,000 units of antitoxin properly administered has obtained all the value from antitoxin which it is possible to give. The City freely gives 100,000 units for a case, after that it expects payment for the antitoxin. We have practically no requests for the larger amounts when payment is insisted upon. We must always remember that the most important fact in the treatment of tetanus is that every minute of delay is important. The use of preventive inoculations is constantly increasing. They are advised wherever there is either a small or large ragged wound which may have been infected with either dirt or dust. One thousand to 1500 units are given subcutaneously and repeated at seven day intervals until the wound is practically healed. When first seen the wound should be thoroughly cleaned and all foreign matter removed.

Scarlet Fever:—This infection is due to strains of hemolytic streptococci. These produce injury through both extracellular and intracellular toxins. Scarlet fever antitoxin serum is obtained from horses injected with a strain of a maximum range of toxin production. The horse should respond markedly to all its different toxins. Such a serum has a marked neutralizing effect on the toxin in the patients during the first few days of the disease in the great majority

of cases of infection. The strains used by us are the famous Dochez N. Y. 5 strain and our number 2^2. These strains though belonging to different immunological groups produce much the same toxins. Both of these strains are used in the injections of our horses to obtain antiscarlatinal serum. And yet while we are getting fine results with this serum in the treatment of most of our severe scarlet fever cases, in an occasional case we seem to get no response at all. This we believe to be due to the fact that these cases are due to different types of streptococci. We are making a collection of the strains of hemolytic streptococci from these cases and are studying their toxins and their antigenic powers, so as to determine their immunological characteristics.

The question of the worth of the bacterial antibody in scarlet fever serum is still largely a matter of theory. We are injecting the whole organisms intravenously into our horses as well as the toxin subcutaneously and we are concentrating and purifying by a method that allows both antibodies, that is, antitoxin and antibacterial antibody, to remain in our final product, but while we believe it is of real value we are not yet sure how much good it does in scarlet fever cases. We do know that bacterial antibodies must be of the same protective type that is causing the disease. This type always corresponds with the agglutinative type. This bacterial type of antibody is a narrower type than the antitoxic type. While in scarlet fever the presence of an antibacterial type that is the same as that of the infecting strain may be of importance in lessening danger from the invasion of the organism, we are sure theoretically that it is of extreme importance in the treatment of erysipelas and other diseases where the hemolytic streptococcus itself invades the tissues.

The serum should have an antitoxic potency of at least 400 units per c.c. The dose in moderate cases is from 10,000 to 15,000 units intramuscularly or 3000 to 5000 intravenously and in severe cases 5000 to 10,000 units are given intravenously. We have lately been trying to give

only 3000 intravenously for the first dose following with a larger amount in 3 to 12 hours. We have had no bad reactions when the serum was given in this way. If the temperature rises after falling and the rash is still present, repeat the injection. In mild cases in which the temperature is less than 102° we do not advise the use of serum, because of the probability of serum sickness following the injection. For some reason antiscarlatinal serum even after being refined is apt to produce serum sickness. *Erysipelas*:—In this disease the types of streptococci are more variable than in scarlet fever. We have had very little personal experience with the use of antitoxic serum, but from the literature and from personal communications we believe that good results are obtained from its use. The antitoxin must match the toxin. This is secured by injecting the horses with toxin obtained from several types. The dosage is the same as in scarlet fever. When an antierysipelas serum is not available an injection of antiscarlatinal serum will usually give equally good results.

Pneumonia:—In diseases due to the pneumococcus we have as yet only an antibacterial serum. Many attempts have been made to demonstrate an extracellular toxin. These so far have not given definite results. The great difficulty in the use of antipneumococcus serum is the fact that the pneumococci divide into so many types. We have now 28 specific types of which about six are prevalent in adults and about 10 in children. As undoubtedly you all know, Types I, II and III have been considered the dominant types in adult pneumonias due to pneumococci. Until recently the pneumococci had been grouped as Types I, II and III and Group IV. Many physicians have not realized that Group IV was simply a name given to the unclassified pneumococci.

In our work upon pneumonia at the Bellevue and Harlem Hospitals, we found that many cases of adult pneumonia were due to several other types. This led Miss Cooper in the Research Laboratories of the Department of Health to classify these pneumococci previously placed in

Group IV, and this led to the development of the numerous types now numbering as stated, 28.

At the present time we only have a supply of antipneumococcus serum for Types I and II. Antiserum for the other types will in time be provided, but at first a careful study must be made as to the value of the serum in the different types and to what extent we can produce polyvalent serums. The usual way of deciding whether a case of pneumonia requires serum and the quantity of serum is to determine the severity of the case. A case with a high temperature and toxic conditions is given a preliminary dose of about 5000 units of a polyvalent Type I and Type II serum. If there is no deleterious reaction to the serum within the course of one or two hours, an additional dose of 15,000 units is given. About every six hours during the first day, an additional 20,000 units of the antiserum is injected.

By far the best method of giving either unrefined or refined antibodies is the intravenous. Intramuscular injections are of value but the slowness of the absorption of serum is a great disadvantage. On the second day if a crisis has not already developed, the serum treatment is continued. At the end of this time the case has either recovered or the value of serum is very doubtful and owing to the expense and the limitation of the supply, the doses of serum are very apt to be discontinued. However, if the case is doing fairly well, but has not recovered, smaller doses of serum may be continued. As a general thing larger doses of serum are required in Type II cases of pneumonia than in Type I cases. The average amount given in Type I cases during the first 24 hours is about 100,000 units while in Type II cases 200,000 units may properly be given.

At the present time the antipneumococcus serum is being refined. Dr. Felton at the Harvard University laboratory was the first one to give us a practical refined antibody

solution which when injected made only occasional chills. Since then Dr. Banzhaf in the Research Laboratory of the Health Department has made equally good preparations by different methods. The present refined antibody solution seldom gives a chill and is seldom followed by serum sickness. The strength of the refined antibody solution is usually between 1000 and 2000 units per c.c. The unrefined serum is supplied by different biological plants in strengths of from 100 to 600 units per c.c. The Government minimum standard requires only 100 units per c.c. and if the units are not printed on the label, the probability is that the anti-pneumococcus serum is of the minimum standard.

The research work done by Dr. Felton and by Miss Cooper as well as the clinical results demonstrate that a unit of refined serum has practically at least all the advantages of a unit of unrefined serum. The purified antibody has the greater advantage of producing many less chills and much less sickness than the unrefined. The disadvantage is that the refined serum must always cost about twice as much as the unrefined because of loss in its preparation and the cost of labor.

The results obtained at the Harlem Hospital in the service of Dr. Jesse G. M. Bullowa and at the Bellevue Hospital under the direction of Dr. Russell L. Cecil have proven in my mind beyond all doubt the great value of Type I serum in Type I cases and the considerable value of Type II serum in Type II cases. Unless the pneumonias are typed at the earliest possible moment we may be giving serum unnecessarily in about two-thirds of the cases. The dose of serum or antibody should be warmed and given very slowly, about fifteen minutes is required.

Poliomyelitis:—For a number of years serum taken from convalescent cases of this disease has been used therapeutically in early cases. Recently in the Research Laboratories, an antiserum has been prepared in horses which is equivalent in value to that obtained from convalescent

cases of the human disease. This serum has been refined by Banzhaf so that it is about three to four times the strength of convalescent serum. Almost everyone is agreed that the serum does no good in cases after paralysis has developed. The majority believe that the serum is of value when given in the pre-paralytic stage of the disease. The difficulty in determining just what advantage the serum treatment gives is founded on the fact that it is very difficult to have controls, because of the great fear of the disease in the minds of people. Every one wants to try the serum if it may possibly do good. Although some doubt the value, the majority believe that the proof is sufficient to make this a suitable treatment.

Dr. Lloyd Aycock in Boston working with the Anti-poliomyelitis Commission has had the greatest experience with the serum treatment and is its most enthusiastic supporter.

Two years ago the following treatment was suggested by a committee of the Academy of Medicine. At once and simultaneously 20 c.c. of human convalescent serum are introduced intraspinally and 20 c.c. in addition intravenously or intramuscularly. On the following two days 20 c.c. more are given intramuscularly or intravenously on each day. Recommendations for the past year were the same but there was some sentiment towards the elimination of intraspinous therapy by some of the physicians. Our experience, however, with animal inoculations makes us believe that at least one intraspinal injection is very desirable.

FACTS AND FALLACIES CONCERNING FOREIGN PROTEIN AND VACCINE THERAPY*

ERNEST E. IRONS

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Methods of treatment of disease, like styles and fabrics of dress, change from year to year and decade to decade and in both, even a brief historical review will demonstrate a continued repetition of older practices somewhat modified to meet new conditions and modes. In matters of dress, which vary from long to short and back again, the original object of clothing to protect the body from cold and injury seems at times to be lost sight of and in medicine newly observed or striking effects lead to the revival or popularization of remedies without due regard to ultimate results, on the assumption that these effects are necessarily beneficial to the patient. The occurrence of the changes is evident; their value to the patient requires careful consideration. The ease of use of the hypodermic needle which makes possible the parenteral introduction of proteins into the body has led to widespread and often uncritical use of this method in the treatment of all manner of conditions and to the drawing of clinical conclusions often without consideration of the natural history of the diseases treated.

Clinical as well as laboratory opinions concerning the method of action and ultimate results to the patient of the parenteral injection of foreign protein, differ widely. Some clinicians use protein shock therapy extensively and believe it to be useful; others are firmly convinced of its uselessness or that the dangers outweigh the possible benefits to be obtained. I must admit that I have some fairly definite opinions, but I will ask you to join with me in

*Delivered October 30, 1930.

endeavoring to lay aside our opinions and consider such of the evidence as it may be possible to present in a few minutes. No matter whether we as a jury can bring in an agreed verdict, or as seems much more probable fail to agree and be discharged, we may gain something by hearing the arguments and what is more important perhaps secure a better appreciation of what is required in the formulation of clinical opinion as to the value of a remedy.

In the study and attempted therapy of infectious disease of the past 40 years, chief emphasis has been on the specific relationship of the cause of the disease and its proposed remedy. The early success of diphtheria antitoxin, and the conceptions of most workers, influenced greatly by the teachings of Ehrlich, tended to direct therapeutic efforts along specific lines, and when treatment by antisera or vaccines was attempted, the causative organism of the disease was used. When specific vaccines failed to yield results expected, it was thought that perhaps by using a vaccine prepared from the identical organism causing the disease in the patient (autogenous) better results might be obtained.

From 1906, the date of Wright's introduction of vaccine treatment, the number of papers on vaccines in medical journals constantly increased until it reached a formidable volume about 1912. From this time on, interest in this form of treatment declined, and the number of papers on vaccine therapy recorded by the Index Medicus steadily shrank until by 1923 they formed but a small part of the articles listed. In 1923 Dr. Hektoen* and I undertook by questionnaire to ascertain the opinion of practising physicians with respect to the use of vaccines. We received replies from 1519 physicians, the groups including members of the special societies of the Congress of American Physicians and Surgeons, physicians in the larger cities of Michigan, physicians of Indianapolis and physicians of

*Hektoen, L. and Irons, E. E., *Journal A. M. A.*, XCII, p. 864, 1929.

New York and Brooklyn. The replies from each of the four groups were in substantial agreement and indicated that the use of vaccines of various sorts had decreased from a widespread use in the years centering around 1912 to a relatively small percentage in 1923. Excluding hearsay reports, we obtained records of 140 instances of harmful results including a number of cases in which death was considered due to the use of vaccines subcutaneously injected. Seventeen cases of asthma were reported to have followed courses of bacterial vaccines, administered to patients who previously were not known to have suffered from asthma.

The verdict of these 1500 jurors selected alphabetically and only on the basis of their willingness to serve, indicated that the great expectations of 1906 to 1912 for the general usefulness of vaccines, had not been fulfilled, as shown by the fact that in all but 5 of 63 different disease conditions for which vaccines had been recommended, the percentage of physicians not using or no longer using them was nearer 100 than 90 per cent.

The span of the rise and fall of the cycle of vaccine popularity was about 15 years. About the time when vaccine therapy in general had passed the peak of its popularity attention was directed anew to some of the reactions which occur in the animal body following the parenteral introduction of foreign protein whether of bacterial or other origin. While non-specific protein therapy has come into prominence in the past 10 years it has been used in some form or other for many decades. In the same number of the *Deutsche Medicinische Wochenschrift* in which in 1893 Fränkel reported on the specific treatment of typhoid fever with subcutaneous injections of typhoid vaccine, Rumpf described the treatment of typhoid fever with pyocyaneus vaccine, on the theory that such non-specific injections could activate dormant and possibly specific powers of resistance. A partial list of measures and substances used to influence the course of infections in a more or less non-specific manner includes fixa-

tion abscesses, setons, blisters, sera of man, horse, sheep, goat, chickens, etc., antiyeast serum of Deutschmann, egg albumin, milk, proteose and other split protein products, tissue extracts and autolysates, leucocytic extracts, vaccines, bacterial toxins and autolysates, Coley's fluid, etc. Just at present, milk or its products, and typhoid vaccine seem to be most popular.

The Reaction

Following the intravenous injection of a foreign protein, there occur rise in temperature and pulse rate, chill, sweating, decrease and later increase in circulating leucocytes. The intramuscular injection of proteins, such as milk, is followed by slight rise in temperature and leucocytosis. Reactions following milk injections have been credited to the bacterial content of the milk, by several investigators.

In patients who had fever previous to the injection, as in typhoid fever or pneumonia, the temperature may fall subsequent to the reaction, and in rare instances may not recur. After the reaction there may be noted decrease of pain and swelling in joints in arthritis, or other clinical changes interpreted as an amelioration of the illness for which the injection was given.

Various theories have been advanced to explain the mechanism of the reaction such as the mobilization of ferments (Jobling and Petersen), the increase in resistance associated with leucocytosis or the stimulation of antibody production by previously sensitized cells. In animals previously stimulated to antibody formation, the injection of non-specific protein sometimes causes a reappearance or increase in specific antibodies such as precipitins (Obermayer and Pick, Hektoen). While there is evidence in support of each of these theories, a complete explanation of the effects of the reaction has not been furnished by the laboratory. Stanley Davidson,* studying the effects of

*Davidson, S., *Tr. Medico-Chir. Soc.*, Edinburgh, 1926-27, p. 21.

intravenous injections of nuclein which produce reactions resembling protein reactions, in rabbits obtained leucopenia followed by leucocytosis, but could demonstrate no therapeutic value as judged by protection tests, using antipneumococcus serum, or by antibody production using agglutination of *B. typhosus*. Other mechanisms suggested to explain observed effects of the injections include the production of vasodilation, and in the case of ulcer of the stomach, of the inhibition of peristalsis.

The Clinical Use of Protein

Even a brief survey of the literature of non-specific protein therapy will reveal an amazing list of different diseases and conditions in which this method has been used and more or less enthusiastically recommended. Included in the list are acute and chronic arthritis, pneumonia, typhoid fever, sepsis, erysipelas, gonorrheal infections, peptic ulcer, bacillary dysentery, encephalitis, general paresis, dermatological conditions, diseases of the eye especially iritis, thrombo-angiitis obliterans, arteriosclerotic gangrene, Raynaud's disease, and nephritis. The length of the list does not make a favorable impression on a follower of Ehrlich. It is reminiscent of the still longer lists of commercial vaccine makers of some years ago and suggests that the clinician is already feeling the lack of laboratory control and guidance which, when available, is so steadying and helpful. The list also suggests a departure from the original theory of non-specific stimulation of resistance to infection as defined by Rumpf in the treatment of typhoid, to include conceptions not strictly immunological, but rather physiological, such as vasodilation, and the inhibition of peristalsis. To accept this evidence en masse without submitting each element to a critical survey in relation to other known facts in immunology, physiology, or clinical medicine would be as unscientific and unfruitful as to deny the occurrence, in certain cases, of the subsidence of fever, the reduction of edema in acute arthritis, or the clinical improvement in

paralytic dementia which sometimes follow the use of foreign proteins.

In some instances of reported therapeutic results, clinical claims have been advanced far beyond laboratory and controlled experimental evidence, and here clinical evidence must stand or fall on its own merits. The empiric method has many triumphs to its credit, but for one triumph there have been countless defeats. Safety, as well as progress, demand that clinical observations be controlled as completely as are laboratory experiments. The fact that the attainment of satisfactory controls in clinical medicine is always difficult and sometimes impossible, does not relieve the observer from his obligation to scientific accuracy.

Hurried Publication

Before passing to a more detailed consideration of the evidence submitted in the literature, one or two general comments may be made. The literature on the use of foreign protein in shock therapy as listed in the Cumulative Index increased from four articles in 1916 to 63, the high point, in 1922, with a gradual decrease to 20 in 1928. The curve resembles that of vaccine literature which began 10 years earlier. Some of these articles are carefully written; others seem hurried and not well thought out, and are admittedly "preliminary reports" in which the writer is cautious in his opening paragraph, braver as he marshals his evidence, and absolutely convinced in his conclusion. May I quote two consecutive sentences which I have paraphrased slightly from an article on non-specific protein therapy—"We recognize that because of the small number of cases (some forty dealing with five diseases) and the short interval since treatment, no definite conclusion can be drawn from results obtained. Our purpose in reporting this series of cases is to point out the usefulness, ease of administration, and applicability of non-specific therapy in several types of disease." In view of the situation described in the first sentence it

is difficult to see how the purpose avowed in the second sentence could be attained except perhaps in the demonstration of the "ease of administration."

Other articles give the impression that if they had been laid away six months they might not have been published, or the conclusions might have been modified.

Clinical Observations

That the intravenous injection of foreign protein produces profound changes in the body is shown both by laboratory tests and by clinical observation. The question we have to answer is not whether such changes occur, but whether they are of advantage to the patient and if so whether the advantage gained offsets any possible disadvantages. We have also to determine whether such improvement as is noted is actually due to the remedy, or whether in the disease in question, similar improvement may occur spontaneously.

Last week a young man was admitted to my hospital service seriously ill with a severe lymphangitis of the arm, which was greatly swollen from wrist to shoulder. He had been sick for two days and on admission his fever was 103° F. The next morning he was much improved, his temperature was lower, and on the third day of treatment the swelling had entirely subsided and the temperature was normal. The treatment consisted of hot moist dressings only, but had vaccines or foreign protein injections or antisera been used, his case would have appeared near the top of the list of brilliant and convincing results.

There are numerous instances in clinical medicine of the favorable effect as to the patient, of one infection on another disease, as illustrated by the decrease in size or even disappearance of malignant lymphoma following an attack of erysipelas. There is much in common between such an event and the result of injection of foreign protein.

Favorable Results

The cutaneous lesions of syphilis are reported to have been favorably influenced by parenteral treatment by milk and by typhoid vaccine, and in some instances complete involution of chronic lesions has been brought about. In some cases of syphilis, Wassermann-fast under arsphenamine treatment, the use of foreign protein injections is reported to have been followed by negative Wassermann reactions subsequent to further arsphenamine treatment. These results have been interpreted as evidence of non-specific stimulation of latent forces of resistance in the body.

In general paralysis of the insane the favorable course with long remissions, following the production of chills by malarial infection or by intravenous injections of typhoid vaccine, are well known and seem to indicate that this method of treatment is useful. By some the fever and by others non-specific stimulation have been credited with the good effects of the treatment. Hanschell* records an interesting case of granuloma pudendi in which the ulceration steadily extended from the genitals over the pubes in spite of various therapeutic measures including antimony potassium tartrate injections. Intravenous injections of typhoid vaccine, producing shock reactions were now combined with further antimony injections in five per cent glucose solution and healing followed. A similar result has been reported by Ormsby in malignant syphilis of the face.

Large spored ringworm infections are reported to have been successfully treated by intravenous injection of typhoid vaccine*.

In certain inflammations of the eye, especially in iritis, improvement sometimes remarkable in its suddenness,

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*Hanschell, H. M., *Transactions Royal Society of Tropical Medicine*, XXII, p. 891, 1929.

*Engman, M. F., *Arch. Dermatology and Syphilology*, XIII, p. 352, 1926.

with reduction of congestion and pain have been observed following foreign protein injections. It is of interest to note that occasionally similar sudden improvement has been seen on the removal of peridental abscesses or after tonsillectomy in iritis. The similarity suggests that the reaction excited by the operation in the surrounding tissues with possible temporary bacteremia is in effect analogous to that following foreign protein.

In arthritis, especially acute arthritis and acute exacerbations of some forms of chronic arthritis, clinical improvement with reduction of pain and swelling are reported after foreign protein therapy.

These few examples will serve to indicate that clinical effects often apparently favorable to the patient, follow foreign protein injections.

Dangers

Protein shock therapy is, however, not without its dangers, although it is but fair to say that considering the large numbers of patients treated in this manner, the incidence of fatal accident, at least of those reported, is relatively small. Some years ago I reported three cases* of fatal outcome, including one case of gonococcal arthritis and one of typhoid fever. While I did not see the patients, I had access to the histories and to the postmortem reports. Punctate cerebral hemorrhages in one, and thrombosis, including thrombosis of the renal artery in another were found. Hench, of Rochester, has recently reported several fatal results in patients under treatment for arthritis. Arterial thrombosis was found in some.

While even the more severe reactions following intravenous injections of foreign proteins usually pass without sequelæ, it sometimes happens that a new and more inconvenient condition is substituted for the original disability, as in the instance cited by Russell of Edinburgh:

*Irons, E. E., *Trans. Assoc. Amer. Physicians*, 1917, p. 91.

"It may perhaps interest you if I tell you of a lady who was subject to attacks of bronchitic asthma from time to time. Years ago she was given what I presume was really protein shock. Some of you may remember that at one time the injection of horse serum was used as a remedy for asthma and in the locality where this lady lived several people had been benefited by the injection of what I take to have been horse serum. The lady submitted to this treatment, with the result that she nearly died of protein shock, and further it had this interesting effect upon her, that ever afterward the smell of a horse gave her asthma. Before that time she had ridden a great deal and was quite a skillful horsewoman."

Modified Views of Specificity

Just how the effects which follow foreign protein injections are produced we do not know. One or several factors including mobilization of ferments, stimulation of antibodies and leucocytes, or the inauguration of chemical changes in the amorphorous or intercellular tissues and fluids, which affect favorably the lesion in the patient, may be responsible. Observations in this field as well as in the field of what we had supposed to be strictly specific therapy indicate that we must take a somewhat broader view of immunologic reactions than has heretofore been required.

We are impelled toward this more liberal view by the newer conceptions of the mechanism of action of therapeutic agents which until recently have been regarded as perfect examples of the principle of strict specificity and were in some cases developed by reason of such theory. Investigations indicate for example that the actions of quinine in malaria, of emetin in infestation with *Amœba histolytica,* and even of arsphenamine and mercury in syphilis, are probably not as was formerly thought, dependent on the direct effect of the remedy on the invading organism, but indirect through the interaction of other substances in the body of the host.

But with this partial casting off of the steadying cable of specificity, we can not safely put to sea without the compass of clinical controls. This compass of clinical control and the natural history of disease is often very difficult to read, but the absence of other guides demands that we study it with greater rather than less care.

The increasing divergence of clinical opinion as to the ultimate effects of treatment, as the number of factors of etiology increases, is well illustrated in arthritis and requires a careful consideration of the natural history of disease.

The Natural History of Disease

Preliminary to drawing conclusions as to the effectiveness of a remedy, it is obviously necessary to know what is likely to be the course of the disease in untreated cases. If we consider a hypothetical disease in which the outcome is known to be uniformly fatal and by a new method of treatment obtain even one or two recoveries in proved cases, we may at once reasonably conclude that the remedy has value.

If we treat a disease whose case fatality is known from years of clinical observation to be 50 per cent, and in a controlled series of cases of sufficient number, obtain by the treatment a case fatality of 25 per cent, we again may conclude that the remedy has clinical value.

The number of observations here necessary to safe conclusions will be much larger, and to satisfy the mathematically minded will probably equal the number of controls which would be required approximately to establish the previously known case fatality rate. Antimeningococcic serum in epidemic cerebrospinal meningitis might be thought of as falling in this category.

As the difference between results in treated and untreated cases grows less, i. e. the effectiveness of the remedy in modifying the outcome less marked, the formulation of

clinical opinion becomes more difficult, the required number of observations and controls greatly increased, and comparison by statistical methods more complicated.

Then, too, the case fatality in age groups, and in epidemics in different years and different localities varies greatly. Diphtheria and scarlet fever are examples. The effectiveness of a remedy is also dependent on the day of the disease when treatment is begun, as is well shown in the treatment of diphtheria by antidiphtheric serum.

Thus in studying statistically the effects of treatment of a disease with reference to case fatality only, in which but two outcomes, recovery or death, are considered, it is at once necessary to subdivide the cases into groups corresponding to those observed in the untreated disease, and a statistical study which at first seemed simple becomes increasingly complex as the number of factors such as age, time of treatment, or epidemic severity increases.

If now we turn to a disease such as arthritis in which there are substituted for the clear cut alternatives of survival or death, such outcomes as relative decrease in disability, relief, complete or relative, of pain, decreased swelling and tenderness, the difficulties of the physician in forming a clinical judgment are increased by the substitution of relative for absolute values, and by the new element of subjective symptoms of the patient whose statements of what he feels and can do are greatly influenced by his state of mind, whether that of hope or discouragement.

The natural history of arthritis presents still further obstacles in the way of clinical judgment. Acute arthritis, due to acute or chronic localized infections elsewhere in the body, frequently heals spontaneously. The swelling, pain and disability disappear and in a few days the joint may function as well as before. In some cases, treatment with foreign protein is said to hasten the return to normal, but whether so treated or not there may be recurrences of the arthritis in the same or other joints. The

clinical question here is whether the benefit of hastened cure, by a few days in some instances, is offset by the failures and possible attendant dangers of the treatment in the others.

The evaluation of the results in relief of pain, disability and deformity which usually pass under the clinical term chronic arthritis is still more troublesome. There may be present the element of infection, but often the immediate cause of disability is mechanical as in osteoarthritis, or in the damage to cartilage of atrophic arthritis, or in referred pain from nerve irritation or pressure.

A man with quiescent and symptomless osteoarthritis of the spine may experience pain following an unusually forceful swing of a golf club. The pain and disability are acute, the underlying cause chronic, and the immediate cause mechanical. He will recover in a few days no matter what is done, provided the treatment does not make him worse.

Examples might be multiplied indefinitely of varying combinations of causes leading to pain, disability or deformity, in a group of patients likely to be gathered together in a clinical report of the results of treatment of arthritis. It must be evident that to draw safe conclusions as to the value of treatment whether by foreign protein or other methods would require more critical judgment than is usually employed or evident in current clinical reports. Failure to group cases by the use of such imperfect standards as are available, or to submit even approximately comparable control groups, often invalidates such meagre conclusions as otherwise might be justified.

Early reports of treatment of disease by any new method are likely to be over-enthusiastic because pioneering requires enthusiasm and further, because the investigator often is entering a new field, inspired by a theory and lacks any considerable background of knowledge of the clinical course of the disease when untreated or treated by other methods.

Even in the more favorable reports of results of treatment of arthritis and iritis there is now and then a note of caution. One of the foremost proponents of protein shock therapy in arthritis finds "that if no benefit is derived after two or three injections it is not probable that further treatment will be beneficial." This would indicate either that the method works only part of the time, or that it is useful only in a selected group of cases. If the latter, then the treatment should be limited to this group, if it can be defined, and a like group of controls furnished.

In discussing the effects of protein therapy in iritis, Benedict and Rucker* remark: "Protein therapy is used with good results in some diseases of the eye. The indications for use and choice of the substance to be used are not clearly established." "In general, little improvement was noted in cases in which the disease had been active for several months or in which there had been previous attacks. The best results were obtained in the patients seen early in the first attack." Again there is noted a group of favorable cases in which from the natural history of the disease improvement would be most likely to be expected.

Less favorable opinion was expressed by Professor Russell commenting in Edinburgh on Davidson's paper, "For myself personally as a physician, I am so greatly impressed with the subtlety of the chemical changes and the chemical variations that occur in individual human bodies that I am almost prepared to believe anything in the way of therapeutic results. I have had a certain amount of experience along these lines and I am not very fond of protein shock in rheumatoid arthritis." "My percentage of benefit and recovery is greater than that recorded by Professor Stockman as obtained from protein shock, and that without protein shock or shock of any kind whatever."

This résumé of some of the evidence for and against the

*Benedict and Rucker, *New Orleans Medical and Surgical Journal*, 81, p. 782, 1929.

use of foreign protein in a few of the many conditions in which it has been used is necessarily brief and incomplete. I have tried to present both sides. The mechanism of the effects as yet lacks complete explanation as well as control by the laboratory. In several groups of diseases the evidence of clinical controls sufficient to warrant conclusions as to the effectiveness of the treatment is lacking.

It must also be noted that in several of the diseases in which clinical effects from foreign protein injections are supported by good evidence, the treatment is designed for use in combination with other recognized methods, rather than to displace them. The clinical effects noted after foreign protein injections in general paralysis of the insane and in other manifestations of syphilis would hardly lead to the treatment of all syphilis by this method to the exclusion of mercury and arsphenamine.

In view of the known relation of chronic infections to iritis, the striking clearing of the circumcorneal inflammation following a foreign protein injection would hardly warrant dependence on this method alone, disregarding other well known methods of examination which may disclose the cause and by its removal prevent recurrence.

In the patient with chronic arthritis there are usually more than one and often several factors contributing to his pain, deformity and disability. The chronic feature of the arthritis may be due to the recurrence of acute exacerbations. Such cases are often associated with chronic local infections, and constitute the group of chronic arthritis which affords examples of relief by the eradication of infection.

The arthritis may be of the atrophic type with swelling and later loss of cartilage and atrophy of muscles, or of the hypertrophic type with proliferation of joint margins and but little muscular atrophy. While infection is believed by some to be one of the chief factors responsible for the former of these two, in both groups other factors including heredity, poor nutrition, metabolic disturbances,

impaired local blood supply, trauma resulting from hard work and from increased weight bearing, to mention but a few, play a large part in the production and progress of joint disease and disability. Pain may result from mechanical causes as in hypertrophic or osteoarthritis and may subside spontaneously.

The permanent relief of pain and disability in chronic arthritis whose etiology is varied and whose course is characterized by spontaneous remissions and exacerbations at intervals of months, seems unlikely to result from the use of one remedy such as foreign protein injections or vaccines, and when improvement occurs following treatment, it seems necessary to reserve some credit for other possible factors.

The evident difficulties of supplying a comparable control series, does not justify clinical conclusions drawn from uncontrolled observations.

In still other disease groups treated by vaccines or milk injections, one function of the treatment seems to be that of a sort of "occupational therapy" in which patient and physician participate, whiling away the time until the natural forces of healing bring about recovery.

Summary

Striking results including numerous instances of clinical improvement have been noted following the use of protein shock therapy. For the most part these have been seen in acute conditions rather than in those of long duration. As a routine and sole method of treatment the case for protein therapy has not been proved. It is necessary here to distinguish from this large group, methods of specific immunization and desensitization employed to relieve the symptoms of sensitiveness to specific known proteins such as those of some pollens and foods. Whenever it is proposed to use protein shock therapy, in a special case, due consideration should be given to possible serious and unexpected outcomes. The present wave of popularity of

injections of foreign proteins for diseases of all descriptions is likely soon to pass, as have other modes and styles.

Even though we as a jury may fail to reach an agreed verdict as to the value of foreign proteins on each count and disease, we shall, I believe, agree that the evaluation of clinical evidence requires caution, and shall continue the care and study of patients with honesty of purpose and with due regard to the natural history of disease.

FACTORS FAVORING THE ONSET AND CONTINUATION OF RHEUMATIC FEVER*

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During the past three decades our ideas concerning rheumatic fever have undergone striking evolution, as evidenced by the change in nomenclature from acute articular rheumatism to acute rheumatic fever, and finally to rheumatic fever. True it is that the older terms still hold, and rightly so when used to describe particular forms of the infection; but too often one is employed synonymously with another. It is unfortunate that with increasing knowledge of the condition there cannot be devised a new term sufficiently extensive to embrace all of its manifestations, yet distinctive enough to separate it as a nosological entity. The introduction of the terms "infectious rheumatism" (1) and "rheumatic granulomatosis" (2) are attempts in this direction; but having only pathologic or bacteriologic significance they offer little if any advantage over the term rheumatic fever, which at least has background in clinical experience.

Objections to the use of this term are twofold: (i) The adjective "rheumatic" to most persons signifies arthritis or muscular pain; and (ii) some of the manifestations of activity—notably chorea—are frequently not accompanied by fever. To this one may reply, first, that the original meaning of the term "rheuma" was a morbid process flowing from one organ or tissue to another; hence it still retains its descriptive value; and, second, that regular consistent use of the thermometer would reveal some degree of

*From the Hospital of the Rockefeller Institute for Medical Research Delivered October 30, 1930.

pyrexia during certain periods of most attacks; therefore, fever still remains one of our most valuable guides of persisting infection.

Another point deserves attention; if the term rheumatic fever is substituted merely for the expression, acute articular rheumatism, our nomenclature has suffered a loss, because the second signifies acutely swollen joints. When, on the other hand, it is used to include all of the manifestations of the infection in the same manner as tuberculosis includes all types of the disease induced by the tubercle bacillus, then does it have distinct descriptive value.

To many it seems well to delete the word "acute" because in the majority of cases the infection is long standing. Only when rapidly fatal, or in those cases with a monocyclic course may the adjective acute be properly applied, but even then we must be certain that the infection has become permanently inactive. For example, we do not picture syphilis as acute even though the roseola disappears within two weeks; likewise it may be better not to use any single manifestation of rheumatic fever as an index of chronicity.

Historically the conception of rheumatic fever began with rheumatic polyarthritis; a century has elapsed since the recognition of the importance of involvement of the valvular endocardium; fifty years ago the nature of the subcutaneous nodule was noted; twenty-five years later its analogue in the submiliary myocardial nodule—the Aschoff body—was described; and within the past decade the extent of the vascular lesions has been appreciated. In the meantime, with an improvement in the general economic state of society, together with extensive use of salicylates the clinical picture has apparently changed. Hyperpyrexia rheumatica has become a medical curiosity, and according to old clinicians rheumatic polyarthritis is less severe. But whether there has been a corresponding amelioration in carditis and chorea one may well doubt. Knowledge gained from contemporary graphic methods of recording

cardiac abnormalities renders difficult comparison with statistics obtained in other ways; but figures such as presented by Ehrström and Wahlberg (3) in Helsingfors indicate that there has been no diminution in the incidence of chronic rheumatic heart disease from the administration of salicylates, and according to recent statistics it still seems that rheumatic fever is the largest single factor in the causation of heart disease (4).

May it not then be of greater value to apply another method of historical approach, beginning in childhood and following the various manners of the unfolding of the infection, rather than to orient ourselves from the disease in adults where it is less frequent even though more acute, and where severe cardiac damage is relatively less common.

But before tracing the clinical course it may be well to reconstruct a background of histopathological tissue changes. What does the microscope show us concerning the nature of the infection? Aschoff's description of the submiliary nodules arising in the loose connective tissue septa in the myocardium furnished a structural archetype to which alterations in other tissues might be compared. The discussion which has centered about this nodule has at times diverted attention away from the fact that other lesions, possibly not quite so regular in their cellular structure, might be just as characteristic. One need only mention the subcutaneous nodule. The important factors to recall are the type of tissues and organs involved, and the manner of evolution of the lesions; one may then attempt to construct from these factors or elements a hypothesis of the nature of the infection.

In the Aschoff body there is a minute central area of broken collagen fibers, surrounded by large cells probably derived from locally stimulated connective tissue. At times there are seen polymorphonuclear cells, lymphocytes and plasma cells; and finally fibroblasts leading eventually to a scar. The subcutaneous nodule shows qualitatively similar tissue injury and cellular response, but with different

quantitative distribution of the component parts; the connective tissue degeneration is often more massive, the groups of large mononuclear cells are more numerous. Frequently a large nodule is apparently formed as a conglomeration of smaller nodules. In places large basophilic mononuclear cells seem to arise from vessel walls. Relatively few polymorphonuclears are present. If now we examine the joints another but related picture appears. The periarticular tendons and ligaments show numerous microscopic areas in the form of nodules or tongues, most having necrotic centers and surrounding proliferated cells. The synovia shows palisading of its lining layer, and minute foci with central necrosis with surrounding collars of cells. Diffuse infiltrations of polymorphonuclears are common. The periarticular tissues are infiltrated with serum which in part contributes to the familiar swollen joint; and there is destruction of muscle fibers at the musculotendinous junctions (2, 5, 6). In other words, the minute focal and vascular lesions about the joints are numerous and exudation is widespread. Involvement of the pleura and pericardium shows similar exudative tendency, but in the substance of these membranes are often foci comparable with the Aschoff bodies. In the auricular endocardium there are similar tissue and cellular changes, but these are arranged in streaks and plaques without interruption in the continuity of the lining endothelium (7, 8a). In the valves on first sight appears another picture, for the endocardium is broken and thrombotic verrucae are often, though not always, laid down at the site of impact of the leaflets. But throughout the substance of the valve and in the chordae may often be seen broken collagen material, proliferative cells and infiltrations like that of the auricular endocardium; at times they are arranged in typical Aschoff bodies. As so beautifully shown by Von Glahn and Pappenheimer (9) and others, many portions of the vascular system are similarly involved. In the aorta focal lesions follow branches of the vasa vasorum; but smaller arteries have areas of end- and mesarteritis, always accompanied by focal destruction of connective or elastic tissue. In the

peritonsillar, nasopharyngeal and intestinal blood vessels Holsti (10) has demonstrated extensive endarteritis verrucosa. In the peritonsillar capsule near the points of attachment of the pharyngeal muscles MacLachlan and Richey (11), Gräff (12) and others have described areas very similar to Aschoff bodies, and also in the tongue about the lingual tonsils. Gräff applies the term "primary complex" to these peritonsillar lesions because of their hypothetical rôle as sites whence the infectious agent is distributed to other parts of the body. He thinks that the pathological condition of the blood vessels supplying these lesions favors such a distribution.

The striking picture of the Aschoff body cells has, moreover, attracted attention away from what appears to be the initial injury to the connective tissue fibers. Von Glahn and Pappenheimer have frequently described the granular broken appearance of these fibers, and many have seen the fibrin-like staining infiltration in the foci; but recently Klinge (13) claims that the primary change is a minute focal "fibrinoid swelling" of the intercellular mesenchymal ground substance; which swelling leads secondarily to a fraying out and altered staining reaction of the collagen fibers and fragmentation of the elastica. He also describes waxy degenerations of individual muscle fibers with secondary proliferation of the perimysium.

It thus appears that rheumatic fever instead of affecting any one set of organs is a disease primarily of the connective tissue, or, in Hueck's (14) words, of the mesenchymal system. Those structures composed chiefly of connective tissue, and specially subject to functional stress and strain and undergoing active motion appear to be the most vulnerable. Interference with the function of these moving structures may, however, detract attention from unobtrusive lesions in other organs, such as recently described by Paul (15) in a rheumatic perihepatitis with characteristic lesions in the underlying blood vessels. Rheumatic vasculitis in the kidneys has been described by Fahr (16), Evans (17) and others; and symptoms of appendicitis, in-

timately associated with generalized rheumatic fever, point to a similar involvement of at least one portion of the intestinal tract. A constantly growing literature on pulmonary lesions in this disease indicates also how the lower as well as the upper portion of the respiratory tract may be involved.

A knowledge of the numerous points and tissues where the infectious agent attacks the body gives us another standard with which to judge rheumatic fever. If so many organs or tissues are simultaneously involved, there is every reason to suppose that they may also be individually and successively implicated. In fact, pediatricians have long appreciated the tendency of children to show first one and then another of the so-called rheumatic series (18); and that not until after the lapse of years might enough members of this series have appeared to render certain a diagnosis. Monosymptomatic signs of disease are difficult of interpretation unless sufficiently characteristic to have diagnostic specificity; for example, the various cutaneous syphilides. But in order to form correct judgment concerning visceral lesions it is often necessary to have concomitant clinical signs or specific laboratory aids.

Unfortunately in the case of rheumatic fever no specific laboratory test is at hand; some of the concomitant, easily visible manifestations, such as tonsillitis, are too non-specific to furnish much needed assistance. But in these very non-specific signs we may possess most important aids to understanding the nature of the infection; and in tracing the life history of rheumatic fever it is essential to note their occurrence and then try to interpret their influence upon the course of the malady.

The causation of many chronic diseases is usually the algebraic sum of a number of factors rather than the exclusive action of any one. Infection is the result of interaction between an animal host and an infecting parasite in which many variables are too subtle for laboratory measurement. Moreover, the study of the life history of

chronic disease in the patient gives us many useful hints as to the nature of the illness, and often furnishes therapeutic indications. For example, we now know that the presence of tubercle bacilli in a body does not necessarily indicate active tuberculosis. Certain environmental conditions favor the spread of the lesions, others favor their regression. Indeed, a study of these latter conditions has furnished us with some of our most important weapons against this disease; and comparable knowledge may conceivably have a similar effect in rheumatic fever.

Geographically the disease seems to be essentially one of the temperate zone. Clarke (19) has recently marshalled most convincing evidence indicating that in the true tropics it is 15 to 20 times less frequent than in Europe. Studies by the Seegals (20) indicate, moreover, that the infection is less common in the southern part of this country; and observations (21) from New Orleans show that when present in the South it runs a milder course than in the North. The ultimate effect of removing rheumatic subjects to hot or dry climates is, however, still a matter for investigation.

Statistics also show that obvious rheumatic fever is from fifteen to twenty times more frequent among the laboring classes than in those forming the bulk of private practice. But many physicians can testify concerning its existence and tendency to progress in patients living under apparently ideal home surroundings. Another viewpoint has been advanced to the effect that among persons in better economic conditions the infection may have relatively more monosymptomatic forms and hence lead more frequently to cardiac damage without obvious general symptoms.

Infants and very young children are relatively free from the disease, and, even though cases appear in children of from two to four years, the curve of frequency of first attacks does not begin its steep ascent until about the age of five or six years. It then rises steadily until the period from

nine to eleven years when it begins to fall; first attacks are relatively much more rare in adults than in children. The studies of Wilson, Lingg, and Croxford (22) indicate, moreover, that children suffering from the infection tend to have fewer obvious relapses after the age of eleven or twelve years. Thus a condition of resistance seems to begin to develop about the age of puberty. But the period of greatest incidence of new cases during the first few years of school life is worthy of emphasis. Is it the result of intimate contact like that seen in measles, or is it due to an age-linked hypersensitiveness? The experience of many observers teaches that the infection is progressing steadily in the hearts of many children while avoiding other organs. For example, Sutton (23) found in the Bellevue Hospital 18 per cent of 427 rheumatic children to have well developed rheumatic carditis without a previous history of either polyarthritis or chorea.

An apparent precursory factor in a majority of cases is repeated infection in the respiratory tract, often in the form of tonsillitis, sinusitis, middle ear disease, or bronchitis. In our experience so frequent has been the occurrence of acute tonsillitis within from one to five weeks of an acute attack that we now date the duration of a given attack from the onset of tonsillitis. But more detailed investigation of the previous state of health of patients usually reveals an earlier history of repeated sore throats, otitis media, or of recurring or almost continuous sinusitis. Not infrequently closer questioning discloses mild joint or growing pains with these upper respiratory infections. Coates and Thomas (24), Coates and Coombs (25), and Vining (26), all report the finding of small subcutaneous granules in a fairly high percentage of school children. Whether or not these are genuine rheumatic subcutaneous nodules is a moot point; but their alleged demonstration by serious students of the disease should stimulate renewed investigation, because extensive painless nodules have been frequently observed in children having no other symptoms of sufficient severity to incapacitate them.

Other conditions in many children preliminary to an acute attack are loss of weight, anorexia, and general signs of mild intoxication. To these Vining has applied the term "toxic debility," and found that many of his rheumatic youngsters had in addition a history of intestinal disturbance of sufficient severity to point to the intestinal tract as an area whence the infectious agent might be spread throughout the body. The greater liability of children of the poorer classes to suffer disorders of malnutrition or to be deprived of certain accessory food substances suggests that possibly these are elements leading to a higher incidence of the disease among such individuals compared with people living on a higher economic scale. Recent studies of rheumatic children in out-patient departments furnish additional support concerning the influence of nutrition in that loss of weight has been found to be one of the most common precursors of a relapse.

Recurrences of symptoms sufficiently severe to be called true relapses are commonly observed in children year after year; but symptoms and signs too mild to attract much attention not infrequently occur between relapses. For example, Shapiro (27) has recently noted electrocardiographic evidence of active cardiac damage in at least 60 per cent of 119 school children following apparently complete recovery from an acute attack; and Levy and Turner (28) have recorded electrocardiographic abnormalities weeks and months before the onset of acute symptoms. Persistent lowgrade leucocytosis, unexplained on grounds other than that of persisting rheumatic infection, is not infrequent. Several of our patients have observed recurring erythema marginatum for months without appreciating its significance until more incapacitating manifestations forced them to seek hospital care, and the continuance of this peculiar rash for weeks or months following subsidence of acute arthritis not infrequently is an index of continuing infection.

Not only are such pictures seen in children, in whom we have learned to expect repeated relapses, but a similar history is not rare in adults, when sought with sufficient care.

For example, a man, aged 33 years, in good circumstances gave a history of acute tonsillitis in 1929 followed by acute rheumatic polyarthritis; then by tonsillectomy. In the winter of 1930 he had sore throat followed by a similar polyarthritis. But more careful questioning revealed repeated pharyngitis for eight to ten years previously, several attacks of sinusitis and recurring pain in the neck and back of sufficient severity to make movements difficult. It does not appear unreasonable to suppose that during the previous years he was suffering from mild rheumatic infection which was not brought to acute intensity until his first attack of severe tonsillitis. Such histories are not rare.

That tonsillitis plays an important rôle in precipitating many acute attacks of rheumatic fever we can accept as fairly well established. Where both diseases are reportable, the peak of the curve of the former antedates that of the latter by about two weeks. Glover (29), in presenting details concerning several concomitant epidemics of these two conditions, advances the theory that they are spread by droplet infection which must reach a certain intensity before the resulting diseases reach epidemic proportions. In one outbreak carefully studied, the carrier rate for meningococci and the incidence of cerebrospinal meningitis and of rheumatic fever, ran parallel; and this suggests that similar influences were at play in causing an increase in all three conditions. With a diminution in crowding there was a disappearance of both diseases, and with renewed crowding there was a return of an equal number of each. While these appeared to be primary attacks of rheumatic fever, one would like information concerning the previous history of the rheumatic individuals. Such questions are raised by the study of epidemics among children with rheumatic heart disease or convalescent from rheumatic fever, such as reported by Boas and Schwartz (30), and Hiller and Graef (31). In the first epidemic reported by the former group there were four cases of bronchopneumonia accompanied by rheumatic carditis, and one of acute

tonsillitis; in the second, although the precursory respiratory infection was not so marked, still acute rheumatic exacerbations developed in six boys in rapid succession. Among 19 non-rheumatic children in the same wards, none suffered from rheumatic fever, while in 22 previously rheumatic subjects 11 developed acute rheumatic fever. In the epidemic reported by Hiller and Graef there were 43 children exposed, of whom 39 probably were previously rheumatic. Within five days of arrival at the camp there were 12 cases of upper respiratory infection, and within five weeks 10 cases of polyarthritis, one of chorea, two of bronchopneumonia, one of acute bronchitis, and one of tonsillitis, pericarditis and pneumonia. Unfortunately the exact relationship of the upper respiratory infections to polyarthritis in each case was not recorded; nevertheless the high incidence of acute exacerbations of the disease in previously rheumatic children is worthy of emphasis, as is also the occurrence of severe pulmonary infection.

Scarlet fever is another disease intimately associated both with first attacks and with relapses of rheumatic fever. Some clinicians state that this disease in previously rheumatic children is practically always followed by acute manifestations of rheumatic fever. This suggests the possibility of comparable influences in all of the above mentioned epidemics, namely upper respiratory infection.

I realize fully the possibility of at least two interpretations of the phenomena described: (i) That rheumatic fever may be due to an unknown virus which may long lie latent in the body, and be incited to renewed activity because of the depressing influence of the acute respiratory infection. (ii) On the other hand, it is possible that repeated and persisting low-grade infections induce or are accompanied by tissue changes too mild to be dignified by the name rheumatic fever, and that only with a stormy acute infection such as tonsillitis, or with invasion of the pulmonary tract by streptococci are the accompanying morbid processes raised above the clinical horizon. In

either case the conditions existing prior to the attack of acute rheumatic fever are worthy of more detailed study than they usually receive.

To illustrate this point let us consider another group in which a contagious element may exist: the family. Since St. Lawrence's (32) report eight years ago showing the incidence of multiple cases of rheumatic fever in a group of families to be as high as that of tuberculosis, there have been several confirmatory studies. It now appears that in a rheumatic family with one case the probability of occurrence of a second case is three or four times as great as in a family previously free from the disease. Although the various factors favoring the development of rheumatic fever may be almost as difficult of analysis within a family as in any other group, the family as a unit offers a promising field for investigation. For example, several years ago we learned that the mother of one of our rheumatic children frequently had sore throats within a short time of the appearance of relapses in the child. Following the removal of badly diseased tonsils in the mother her attacks of sore throat ceased and since then the child has been free from recurrences. Last winter a boy was admitted to the hospital with the following recent history of acute infections in himself, his mother and sister:

1st day Onset of "grippe" in patient and sister.
5th day Patient better; sister developed rash.
8th day Mother developed "grippe" with severe pain in back; sister recovered and lost rash.
12th day Mother recovered.
14th day Patient developed fever and beginning polyarthritis.
16th day Patient had evidence of severe myocarditis.
19th day Patient had signs of pericarditis.

Such a history of contagion reminds one of the concomitant respiratory infections in the epidemics mentioned above, and suggests the possibility of atypical non-diagnostic manifestations in the sister and mother. Indeed, a correlation of all of the illnesses of the members of fifteen rheumatic families by Paul and Salinger (33) has already yielded important data along these lines. They have shown

that both primary and secondary attacks of rheumatic fever in certain members of a family have been accompanied by the simultaneous appearance of recognizable rheumatic fever in other members of the family, and not infrequently by the appearance of such non-specific affections as sore throat, bronchitis, bronchopneumonia and skin rashes. They found in addition that the disease spread more frequently to the children under twelve years of age than to the older children and adults. Another striking feature among these families was the frequency with which so called non-specific respiratory infections occurred before the appearance of characteristic rheumatic fever. If an extension of this type of investigation yields similar data, we shall be in a position to formulate preventive measures not heretofore applied. Indeed, the information already available from the several reports above reviewed together with those of Andrieu (34), Grenet (35), Irvine-Jones (36) and others suggests strongly the communicable nature of the infection. The time when health authorities will recognize this feature of the disease and attempt to assemble data compiled from compulsory notification may be nearer than we can now foresee. The numerical and economic importance of the problem far outweighs that of poliomyelitis, encephalitis, leprosy, and many other reportable diseases.

One more feature deserves attention; the hypersensitiveness of patients with rheumatic fever to streptococcal products, which has been found by most observers to be higher than in any other disease. One must admit that such hypersensitiveness is found in many non-rheumatic persons; hence these skin tests have not diagnostic specificity. But it has offered a possible explanation of certain peculiarities of the disease (37). Mackenzie and Hanger (38), Kaiser (39), and Ando (40) have all shown this type of hypersensitiveness to be rare or absent in infancy and to increase in relative frequency with each half decade up to the period of adult life. In Duckett Jones' (41) experience over 95 per cent of rheumatic children have positive reac-

tions to a filtrate of a single strain of indifferent streptococci. Derick and Fulton (42) have recently found skin hypersensitivity to hemolytic streptococcal nucleoproteins in 88 per cent of rheumatic children between six and ten years of age compared with only 12 per cent in non-rheumatic children, surely a most significant difference, when it is noted that 88 per cent of their entire group of rheumatic fever patients gave positive reactions. It thus seems that hypersensitiveness to streptococci which appears with advancing years in many individuals occurs much earlier in rheumatic fever patients. Probably the repeated respiratory infections already so frequently mentioned are factors in conditioning a high sensitivity to streptococci; and it does not seem improbable that the condition recognized as acute rheumatic fever is incited by intense, focal infections such as acute tonsillitis, or otitis media—both due to hemolytic streptococci—occurring in already somewhat hypersensitive bodies. On the other hand, it must be recognized that we do not know definitely whether the relationship between streptococcal hypersensitiveness and rheumatic fever is causal or merely concomitant. Its existence, however, gives us a definite point of attack (43), for could we influence it in one direction or another we would have an index with which to judge the effect of certain therapeutic efforts.

Summary

Rheumatic fever is economically one of the most important diseases, not only because of its acute manifestations, but also because of its rôle in the production of between 30 and 40 per cent of chronic cardiac disease in the latitude of the North Atlantic States. Microscopic findings indicate it to be a wide-spread disease involving by preference mesenchymal structures or mesenchymal portions of parenchymatous organs. Physiological stress and strain appear to favor localization of its manifestations, although it may be locally active without giving rise to symptoms; and various vulnerable organs may be either simultaneously or independently involved.

A number of factors appear to have causative relationships. Climatic conditions such as exist in temperate zones in winter favor its development; while sunny dry summers and tropical weather inhibit or prevent its evolution. Among the poorer classes it is from 15 to 20 times more prevalent than in persons better housed and fed. Malnutrition and mild toxic states are frequent precursors of characteristic attacks. Most patients, both children and adults, give a history of repeated non-specific infections of the respiratory tract, tonsils, sinuses, or middle ear, extending over several years, before a typical attack of rheumatic fever is ushered in by a severe focal infection. Persons in intimate contact with patients during acute outbursts of rheumatic fever not infrequently suffer simultaneously from upper respiratory infections, or from typical rheumatic fever; hence there seems to be a distinct communicable factor favoring its spread. Because chronicity and relapses are so frequent, and crippling cardiac damage is of such gradual evolution, and finally because laboratory tests often reveal activity in periods between attacks, it seems justifiable to consider the infection to be characterized by long periods of preparation or sensitization of the tissues, the result of repeated mild infection before a more intense focal infection sets off the violent explosion recognized as acute rheumatic fever. Similar mild infections, moreover, apparently favor the continuation of true rheumatic activity in viscera already involved. It seems logical, therefore, to regard these preparatory periods and mild chronic infections between acute outbreaks as essential parts of the morbid process; hence our therapeutic and prophylactic efforts should be directed against them as well as against the more acute manifestations of the disease.

NOTE—While this article was in press the monograph (44) of Coburn appeared which presents much valuable additional evidence concerning the chronic and contiguous nature of rheumatic fever; its geographic distribution; the high degree of cutaneous sensitivity of rheumatic fever

patients to hemolytic streptococcal nucleoprotein; and finally, a striking parallelism between an increase of hemolytic streptococci in the upper respiratory tract and relapses in patients with the disease. He apparently wishes to designate the malady as the "rheumatic state" and only recognizes "rheumatic fever" when it is diagnostically clear cut.

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THE CONTINUED EDUCATION OF THE DOCTOR*

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The invitation to address you, which I had the honor to receive from Dr. Marcus, suggested that I might speak along lines similar to those presented to The New York Academy of Medicine in the Presidential Address last January.

In the course of that discussion, it was stated that some of the difficulties of present medical practice might be relieved by a return to an earlier practice when every family had a definite medical adviser who was trained in the field of general medicine with a sufficient knowledge of special fields to know when the condition would be benefited by the care of a specialist. This comment attracted the attention of many physicians and laymen. It is, of course, no new idea. The fact that it was seized upon as the main text of an address dealing with various matters emphasizes still more that it has a great hold upon the imagination.

It will be my endeavor to present the subject in such a way that you will recognize that the family doctor is essential in the continued education of the doctor. I shall confine myself to a consideration of the situation as it exists in and around New York City. But you will recognize that the conditions discussed are not local in their application.

There is little doubt in the mind of any one who is giving thought to matters of health, that the time is opportune and even demands an accurate evaluation of all the factors concerned in establishing and maintaining the health of

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the individual and the community. Paramount among these factors is the one that any solution of medical service to a community is in the last analysis dependent upon the science of medicine and on its efficient practice. Attention to organization, economics, distribution, and all other factors is of value only as it serves greater efficiency in medical practice. It may prove of value to review how The New York Academy of Medicine seeks to serve these ends.

The Academy has three fundamental aims: the maintenance of an inclusive medical library, the advancement of public health interests, and the advancement of medical education. It is the latter of these which particularly concerns us at this time. And it is that phase of medical education which pertains to the doctor after he has received his degree and license to practice his profession which we would especially emphasize. But the Academy itself is in no sense a post-graduate medical institution. We have no faculty; we have no students enrolled in our courses. Nevertheless every activity which the Academy carries on has for its object the continued education of the doctor—the aim to improve the practitioners and their service to the community.

For several years a Committee on Medical Education has been charged with this special field and it has done splendid work in providing lectures and practical demonstrations at the Academy.

This committee is probably known to many of you through the Bureau of Clinical Information and its publications detailing the opportunities for study or demonstration in the various hospitals. All these activities, we have every reason to believe, are of value to the doctor in New York, whether residing there or making a transient visit. But they lack one essential thing: they are not parts of a whole; their relationship oftentimes is not apparent and oftentimes nonexistent. Within the past half-decade the Academy has reached a full realization that, if it is to enjoy its privileges, it should accept its responsibilities.

There was brought to our consciousness the need of a careful study of educational opportunities. From whatever angle the question was approached, one constantly returned to the fundamental point that a great wastage was taking place and that the recent medical graduate was too much at the mercy of chance for his continued education.

Our first approach was to determine the qualifications which would properly entitle a man to be considered as competent in a given field. A subcommittee was asked to attack this phase of the problem of specialism and has spent much time in hard, conscientious work. It has evolved a program for the minimum training and experience which a man should receive before he can be graded as qualified in a specialty. This was not so difficult to do because it was somewhat in the nature of an academic pronouncement. The weakness of the position became apparent, however, when someone raised the question as to how the individual doctor, who desired to become proficient in any particular field, could find the necessary opportunities to meet the academic requirements. A review of the courses given in the various hospitals of the city, which had received the endorsement of the Academy as being of value, showed that few could fully meet the requirements of training men in a really efficient way. This led the committee to the following statement of opinion.

"In order to raise the standard of their own groups certain national organizations are demanding definite educational and practical requirements for admission to membership. This certainly prompts young men to seek the necessary proficiency in order to qualify, but the requirements in themselves do not provide opportunities for study. Such opportunities at present exist only to a limited degree. Only a few universities have established complete departments or separate courses depending on their facilities. Several of them offer an advanced degree for work accomplished. A large number of hospitals, however, especially those devoted to the specialties, have established

residencies of from 1 to 2 years which serve as training for that specialty. These various efforts are very worthy and in their particular locality those institutions are doing commendable work. The opportunities thus offered, however, are inadequate for the total number of men who want to, or who should, take advanced courses.

"It has seemed to our committee that in order to actually help along the cause of medical education, especially in reference to advanced or graduate medical education, it is more important to provide opportunities for study than to make demands on the young medical man. On an undergraduate, we do not simply make demands; we provide the medical school in which systematized courses are offered which make it possible to pursue an orderly, well arranged course of study, and then at the end of four years we demand that he successfully pass in the prescribed subjects. In the same way interns are provided with hospitals in which they continue their studies under the direction of members of the attending staff. For the young man who wants to become a specialist, however, no such definitely arranged, orderly courses are provided. He has to shift for himself and try to pick up whatever knowledge he requires to perfect himself in his chosen field.

"It is time we assume a helpful attitude toward these men. We should provide opportunities for study and practical work, carefully and systematically arranged, and after that has been done we may make certain demands on them.

"With this idea in mind we may ask ourselves, and ask of this city, what we have done to further the cause of graduate education? Have we made the best of our opportunities? If we have not, what steps shall we take to utilize the clinical resources of New York City for the ultimate benefit of the people, not only of New York City but of a large part of this country?"

This extract from their report goes directly to the fundamental point in the discussion. The question being

raised, it immediately becomes our responsibility to attempt to find the correct answer. For this purpose the Board of Advanced Medical Education was set up, consisting of representatives of some 30 hospitals in New York City which had shown themselves sympathetic to the idea of taking part in the formal education of our medical graduates. These representatives have met on several occasions and have individually worked on the problem of providing adequate facilities so that the largest possible number of medical graduates can be guided and aided in their continued education, but with the thought of the specialist always uppermost.

You will recall that the original aim only included formulating qualifications for a specialist and expanded into finding opportunities whereby the doctor who was desirous of becoming a specialist could be provided with them. At this stage it became quite apparent that any plan for the development of specialists which did not take into consideration the development of what was recognized as the general practitioner, was lacking in an approach to the core of the matter. No one who has written upon, discussed, or given real thought to the problem of specialization has failed to emphasize the grave danger that lies ahead of the medical profession if its young graduates are launched into special fields without a broad fundamental training. A training which, in fact, will make of them competent general practitioners, even though of limited experience, able to understand and take care of the major portion of the illnesses of the community efficiently. In spite of this clear understanding, it is quite apparent that the trend is more and more toward early specialization without sufficient basic clinical training. The Academy therefore came face to face with the entire problem of the continued education of the young graduate from the time he receives his license to practice until he is established in his profession, well qualified for general practice and, if he so elect, for specialization.

The magnitude of such an undertaking was immediately recognized. The question at once was raised: Is the time opportune for attacking such a job, and if it is, is there any hope that the Academy of Medicine is in a position to lead in its successful conduct? We have not tried to evade the issue and after careful consideration we are now launched upon an attempt to find the proper formula whereby such a goal may be reached.

During the two years that this situation had been developing, another thought had taken shape in the minds of those who are devoting their interest and time to this general subject. This thought related to the question as to whether within our own organization we could take an immediate forward step. Other committees working on this phase of the project brought forward a plan for a change in our internal organization which has received the approval of the Academy.

Heretofore, newly elected members of the Academy organization, as mentioned above, have been designated as Fellows and have had the privilege of associating themselves with all the activities of the Academy and of taking part in the administration and proceedings of all its Sections. No attempt was made to carry these men forward in their educational development as individuals except as they, themselves, saw fit to develop; and the Academy recognized no change in their status from the time of their admission. Under the new plan, a newly elected individual will become a member of the Academy. Upon his request, he will be assigned as a participator in some one of the Sections. The activities of this Section represent the line of development along which he particularly wishes to travel. He is entirely free to enjoy all the coördinate educational advantages that other activities of the Academy and other Sections may afford. In fact, he will be encouraged to avail himself of them. At such time as any such member demonstrates to a specially selected committee, of the older men of his Section of choice, that he is proficient in his field, as proved by such tests as this

committee sees fit to establish, he will be recommended for *promotion* to Fellowship in that branch and, for example, become a Fellow of the Academy of Medicine in Otology, General Medicine, or General Surgery, etc. Having done this, we are now faced with the necessity of procuring the facilities whereby the young man may carry forward the needed development, for his promotion.

But the membership of the Academy includes less than 2000 of the total 12,000 practitioners of medicine in the metropolitan district. If the individual who has attained the rank of Fellow in any particular field receives, thereby, any advantage, it is only fair that the Academy should extend the opportunities to gain this advantage to members of the profession who are not on the Academy roll. Similar opportunities should be furnished to all young men of the profession, and if they so desire, the Academy should certify these young men, whether or not members, that they have attained that degree of proficiency which, in the opinion of the Academy, entitles them to recognition in a particular field. It may well be that the Academy never will have to render this service; that the doctors not belonging to the Academy will have no concern as to whether it certifies to their qualification or not. The situation is not altered thereby because the responsibility to provide educational opportunities is none the less a real one.

It is evident that the continued education of the doctor can only be approached through a consideration of the needs of the general practitioner. In other words, the latter is of necessity from the standpoint of sound pedagogy, the starting point.

In New York City there is well over a hundred million dollars invested in the education of medical students and the advancement of the medical sciences, incidental thereto. When these same students become doctors of medicine and receive a license from the state, they are entirely dependent upon their own initiative as to further events. After that time neither the university nor the state con-

cerns itself with their development. They are legally endowed with full authority to undertake the care of the sick. No one is concerned as to whether further training or experience qualify them to minister to the pregnant woman, extirpate her uterus, determine the metabolic rate caused by a dysfunctioning thyroid, or trephine the eyeball for glaucoma.

In blunt English, it is no less than foolhardy to neglect the continued education of the doctor at this most critical period of his development when a reasonable amount of effort and the expenditure of a relatively small sum would guide him to a real orientation of his abilities.

While nearly every medical student, upon receiving his degree, takes a hospital internship, some do not and it is a matter of unconcern in the eyes of this state whether they do or not. When they do, however, the education received as an intern is largely a matter of chance. It is well within the truth to say that both the board of trustees and the medical board of many of our hospitals are more concerned with what the intern gives to the hospital than they are with the education he receives from it. If he be a man of unusual attainment and ability to absorb information, his associations as hospital intern are of the utmost educational value, provided the type of work done by the hospital staff is of a high grade. If, on the other hand, he be of average ability, it is quite probable that he will be so overwhelmed with the routine work which is required of him that he will have little energy left to look after his educational interests. A number of interns of more than average ability have acknowledged that they are so rushed and fatigued by carrying out their prescribed duties that they have little incentive to undertake serious study. They, of course, pick up a very considerable amount of practical education but a moment's consideration shows that, under proper arrangement, the time spent in the hospital could be made of much greater value to the intern. It is true that the American Medical Association, the Association of American Medical Colleges, and the American College

of Surgeons, have set up certain standards to which hospitals must conform if they receive accredited standing as suitable institutions for internship, but this represents only a beginning.

It is well within my memory when the leading hospitals of New York City looked askance upon the admission of undergraduate medical students to their wards and demonstration rooms for educational purposes. Thirty years has seen an enormous change in this direction. When once it was pointed out to the trustees of these institutions that they had a definite obligation toward using the facilities of their hospitals for the education of medical students, they welcomed the innovation. Not only did they welcome it but worked hand in hand with the universities. They sought and obtained enormous sums of money for the specific purpose of granting such education. To such an extent has this idea developed at the present time that every board of hospital trustees feels the need of some affiliation with a teaching institution and the more intimate these associations can be made, the better satisfied are the trustees.

If this change of front was accomplished in the period of less than a generation, there is every reason to believe that when the attention of hospital authorities is definitely called to their further obligation toward the educational needs of these same men, the response will be equally satisfactory and effective. The Board of Advanced Medical Education already mentioned, is a first step in inaugurating this program.

Through definite effort and hard work by the American Medical Association, the Association of American Medical Colleges, the stimulation of some of the Foundations, a tremendous step forward has been made, in giving a satisfactory education to the aspirant for the degree of Doctor of Medicine. It is now equally important that forces should be set in motion which will give definite form to granting to this aspirant opportunity and guidance

through the years subsequent to his receiving his doctorate of medicine.

I imagine that if any one of you were casually asked to lay down a program for the satisfactory, continued education of the doctor through the first five years of his entrance into the medical profession, you would feel that a free evening would permit you to satisfactorily answer the proposal. From a rather distressing personal experience and close observation of the experience of others, I am inclined to believe that the result of your quiet evening would be to find yourself in rather a hopeless maze. In other words, it has become obvious to those of us who have put a good deal of thought and effort upon this subject, that the problem is hardly less difficult than that which confronted those who wished to put undergraduate medical education on a sound and more or less systematized basis. This was the work of many able men over a period of years. It is quite probable that the same amount of energy must be expended in meeting the present problem. The first step, obviously, is to demonstrate the need for a careful review of the problems, and subsequently the formulation of plans which may reasonably be expected to lead us to our goal.

It is requisite that a careful evaluation be made of the degree of proficiency to which our graduates arrive, five years after their graduation, and the roads along which they travel during these five years, in order that we may reach an understanding of the relative proficiency of result and efficiency of method. The hospital internship, as already pointed out, needs careful revision as the first step. In some cases the intern has an opportunity to get a fairly broad vision of the field of clinical medicine. He comes in contact with many types of cases, with men of stimulating minds; and he has an opportunity to compare methods of arriving at correct conclusions and obtaining definite results. In other cases, he is placed upon a treadmill where, by violent physical effort, he finally reaches

the top and falls over the other side with a vision that has been cramped within the narrow confines of one field. In saying this I am not referring to the hospitals for special service only, but to those covering more or less broad fields where the intern is confined to a so-called "straight service." In still other institutions the whole system connected with the intern's education is one of wasted opportunities. It is rare that any one makes it his concern to see that the intern gets a fair deal and often no one sees to it that the intern really renders a service that prevents his falling into sloppy, careless methods. He passes out of the hospital door with a diploma bearing the stamp of approval of the hospital authorities; a document in many instances of real value and representing hard endeavor and definite attainment; in other instances valueless. What then? He may, by fortunate association, unusual ability, or pleasing personality, find himself sought after and encouraged, placed in positions where his growth is provided for and where he is stimulated toward his continued education. On the other hand, lacking these fortuitous advantages, he finds himself in a precarious position of unfruitful struggle. Possessed of energy and initiative, those belonging to the latter group with much wasted effort ally themselves with various undertakings, and valiantly push forward by the trial and error method toward better things. During this period the great majority of them of necessity must be chiefly concerned with earning an income. In many instances they are forced to accept associations that are of little educational value and giving little professional experience, in order to meet the expense of existence. This method of competition of course has the advantage of bringing to the top those of real ability and sound fundamental training. Rarely does such a one fail of ultimate attainment, of good education and real proficiency in his profession. From this and the first group many of the leaders come. But what of the rank and file who are endowed with sufficient inherent ability and energy, with proper encouragement to become the back-bone rather than the head of the medical profession? Lacking the qualifi-

cations for leadership, they trail behind and are gradually content to accept what seems the inevitable, and struggle to form a clientele to which they give a service comparable to their narrow opportunities and from which they receive a meager return.

I do not believe I can be challenged when I say that this group falls far short of reaching that degree of proficiency of which they are capable, under proper guidance, stimulation and fair opportunity. Is it asking too much that the head be concerned with the strengthening of the backbone? Should not those who enjoy the privilege of leadership be greatly concerned and lend more than a helping hand toward this object?

This situation is also responsible for a great many of our younger men launching themselves into a special field with very inadequate previous training, because by this simple device they are able more promptly to get financial return and feel a certain relief from economic burden. The public, as matters at present stand, is of necessity poorly informed as to the actual qualifications of many designating themselves as specialists. The tradition, deeply rooted in the human mind, that special service is of special value and must accordingly be paid for at special rates, yields a higher immediate financial reward to these men than to those who endeavor in broader fields. This system, I repeat, is tragically wasteful and unsatisfactory. We, as members of the profession are naturally loath to face the fact squarely that many of our colleagues are, of necessity, lacking in the competency that is obviously desirable. In doing this we are open to the accusation of disloyalty and of tending to inculcate in the public mind a lack of confidence in the profession which we hold in high honor. Some of the results and pronouncements which have been made in connection with the various studies to which I have referred have brought forth this criticism rather severely. I believe that this is begging the question. Until the profession is willing and able to devise a plan and demand the execution of that plan, whereby those of its mem-

bers are encouraged and helped to the utmost to attain their fullest development, and whereby the public may have, through standards set up by the profession itself, access to information which will permit them to know who are the well trained, carefully prepared conscientious doctors, we cannot escape just criticism. The considerations here set forth, I believe, have established the need for continued medical education which I stated was obviously the first step.

Reference has been made to the unsatisfactory and even chaotic condition of internships as at present existing. It is here that the young doctor gets his first real independent responsibility. It is here that he gets his first continuous opportunity to observe illness in its entirety. It is here that he is confronted with the actual application of the principles learned in the basic sciences to which he had some introduction in the clinical teaching of his pregraduate days. It is of the utmost importance that he should be under the tutelage of men who are concerned with his development; who feel a keen interest in aiding this development and who take a satisfaction in training those who will subsequently fill their places. It is therefore essential that the professional staff of the hospital shall be organized as a teaching unit in the same way that the faculty of the medical college is organized as a teaching unit. Much thought and constructive effort has been placed on the development of the college curriculum and as at present administered in this country we have a confidence that it is reasonably sound pedagogically. The same thought must be given to developing the hospital organization in the same way.

It would give me the utmost satisfaction if I were able to present to you an ideal hospital curriculum including training in the various clinical fields, and the laboratories, as well as giving due respect to the basic sciences and literary attainment. Unfortunately, I find myself totally unable to do this, but it is my earnest plea that this question receive thoughtful consideration and constructive

effort on the part of educators and hospital administrators. At the present time I am particularly concerned in pointing out to you that it is a crying need and that its adequate solution is perfectly possible, as is proved by attention to what has been accomplished when the medical profession sets its mind seriously upon the solution of such a problem. I have already alluded to two examples, one having to do with the tremendous improvement in our undergraduate medical teaching; and the second with the enthusiastic coöperation of the hospital in this program when the need was pointed out.

It is our hope that we may be able to present the problem of the continued education of the doctor; its present unsatisfactory position; the crying need for its correction and the hope for definite results in such a way that the ways and means may be found to give this whole subject the study that it requires and the help that must be extended to it if advantage is to be taken of the opportunities that lie before us. In this way, at some future date, it will be possible to present to you that well thought out, efficiently functioning curriculum for the hospital interns which I have just regretted I cannot lay before you today.

Having carried our recent graduate through his internship which, if this plan succeeds, will be a direct continuation of his undergraduate education, the even more difficult problem confronts us of guiding him through the subsequent three to five years. A certain number will continue their studies within the hospital organization as an integral part of it, in the position of residents, or other members of the professional staff. Such will inevitably be a part of the machinery having to do with the problem of interns which we have just discussed. These men will be the strong individuals who are endowed with those qualities that fit them for leadership. The number that can so continue their training is strictly limited and constitutes a small portion of those who have passed through the preliminary stages. What will become of the others assuming that they have actually received sound educa-

tional value while serving as interns? The time has not arrived when they should be left to shift for themselves in a hit or miss fashion. In the 130 hospitals in New York City of which 30 have shown a sympathetic attitude toward this whole subject by organizing themselves into the Board of Advanced Medical Education, there are sufficient opportunities to allow educational advantages for practically the entire number of younger doctors in the city who, at the stage of development to which they now have been brought, have demonstrated their fitness to go on in the profession.

In recent years, not only in New York but in other communities, there has been much agitation over what is loosely known as the "open hospital." A great deal of discussion has developed along poorly thought-out lines and has resulted in the advocacy of hopelessly impractical and unproductive hypotheses. Underlying this, however, is a perfectly sound central conception; namely, that it should be possible to so organize hospitals that their educational facilities shall be available to, as nearly as possible, the entire community. Not infrequently the discussions have centered around the economic injustice of limiting the facilities of the hospitals to a certain so-called favored few. In my opinion, this is unsound and not helpful. I am strongly of the opinion that if we will furnish the educational opportunities to our doctors and place before them a clientele which is satisfied that it will receive competent care, individually and collectively; and that the public health interests will be adequately considered and safeguarded; then automatically the economic problem of the medical profession will be largely solved. The public will pay for such service gladly, and in sufficient amount so that every member of our profession who thoroughly and conscientiously trains himself, will have ample opportunity to be paid adequately for his effort. I cannot expect full agreement with this conception. But I am impressed with the fact that, except in times of great stress, those members of the profession who have had adequate educa-

tional opportunities and have utilized these to the best advantage, receive sufficient economic support for the services they render to become respected and self-respecting members of the community. Barring extraneous misfortune, those who find life too confined and cramped because of economic pressure, have failed in one or the other of these requisites.

Our program then, is somewhat as follows: A careful appraisal of all the internships at present in the various hospitals of the metropolitan district should be made. We already have information as to the number of these; the number of beds provided; the fact as to whether they are so-called straight or rotating service; and in a very general way the type of service that is offered. We must be informed, by an analysis made by trained and competent observers, as to actual details. It will be necessary to study the various hospitals and learn the value of the educational training that the interns are receiving. While such study is in progress, material will be gathered to indicate how the various services can be best utilized with the facilities at their disposal to meet the object we have in mind. Since these hospitals are exceedingly varied in their activities, organization, financial status and so forth, it is quite obvious that each one will have to be considered as an entity. It is probable, however, that they will fall into very definite groups and that these groups will be able, more or less, to follow one systematized plan. The material at hand from such an investigation will give accurate information as to how the laboratory service, and even the basic medical sciences, shall be fitted into the general picture. With such complete information, one would be in a position to know the type of educational training each hospital can be developed to offer, and where needed a definite program could be formulated as a basis for obtaining the requisite financial support.

The hospitals of New York afford a large number of residences, which are filled by men who have received the training of an intern. Many of these are excellent educa-

tionally and are much sought after. The majority of them are in special fields and, as has already been learned, they are often held by men who have not had as much training in general medicine as is desirable. In any case the number of such residences must be limited and will only provide educational facilities for the more favored and more competent. Therefore, the problem of helping the rank and file of our younger doctors, immediately after they have left their internship, is one of utmost importance in the whole plan. We know that in the metropolitan district and probably in every community there are vast educational facilities that are inadequately used. This applies particularly to those institutions which are not actively engaged in undergraduate teaching. Even in many of those, the outpatient department fails to yield more than a small part of its educational advantage. Outpatient departments properly organized and giving true value to education are the very best places in the world for a young man to get invaluable clinical experience. Imperfectly organized and badly administered, they may well be the graveyard of his aspirations and the actual grave of his previous, carefully acquired scientific trend.

It seems to me that the most vital element in this plan is concerned with creating the will to teach. With this developed, there can be no question that a means of giving the earnest young doctors full educational opportunities will be found.

While the use of the in-service of the hospital to cover this special period is more difficult, I am of the opinion that the careful study we are advocating will also find opportunity for a greatly increased use of this service.

You will have recognized the validity of our being staggered by the magnitude of the undertaking we have in mind, when its full import was presented to us. The fact that we have already received, not only a sympathetic, but a really enthusiastic response from 30 of our hospitals and that a number of them have actually set up splendidly

functioning plants, encourages us to believe that the will to help already is in existence. This encouragement gives us the impetus to go forward. The consummation of the plan cannot be reached during the period of activity of myself or of many of the men who are working with us. But we intend to carry it forward far enough so that the need will be fully demonstrated and the road to follow plainly blazed.

AWARD OF ALEXANDER COCHRAN BOWEN SCHOLARSHIP

The Alexander Cochran Bowen Scholarships for this year have been awarded to Dr. Henry B. Kirkland and Dr. Charles W. Layne. The Scholarships amount to $1900 each and are intended to provide for one year of foreign study in a clinical subject. They are open to recent graduate interns, men or women, of hospitals in New York City which accept charity patients. There were twelve applicants for this year's Scholarships.

Dr. Kirkland obtained his A. B. degree from Princeton University and graduated in medicine from Cornell University in 1928. He served a two-year internship on the Second Medical Division of Bellevue Hospital and is at present concluding a year as Assistant Pathologist in the same institution.

Dr. Layne graduated in medicine from Emory University in 1928. He served a two-year internship on the Fourth Medical Division of Bellevue Hospital and is at present at the Craig House, Beacon, N. Y.

EXTENSION TO ACADEMY BUILDING

The report of the Committee on Activities adopted by the Academy in January 1929, outlined the present and possible future activities of the Academy, and stressed emphatically the importance of an extension to the present building. It had been recognized when the present building was constructed that only the activities then under way could be housed in it. The report therefore urged the importance of an extension and subsequently the Council authorized the appointment of a special Committee on Gifts and Bequests of which the President was Chairman, to secure additional funds for an extension and additional endowment.

In June 1930, a letter was sent to Mr. Edward S. Harkness, asking if he would be interested in making a grant toward the construction of an addition at a cost of $350,000, or in making a donation toward $400,000 of additional endowment. The Committee was very much gratified to hear from Mr. Harkness in July 1930, that he would be glad to give the sum of $350,000 for the construction of an addition, provided the Academy was able to secure $400,000 of endowment prior to July 1, 1931.

$400,000 Secured.

It was reported to the Council at its meeting on May 27, 1931, that $403,137.92 had been obtained, which includes a tentative grant from one of the Foundations of $50,000 or more, which has not yet been officially confirmed.

At the January meeting of the Board a Building Committee was appointed, consisting of Drs. Duel, Pool, Niles, Cohn, Hartwell, Williams and Malloch. Messrs. York and Sawyer were shortly instructed to prepare preliminary drawings for an extension. The architects prepared two plans, one for the construction of an addition over the present auditorium which would extend up to the height of the

present main building, including two new stack stories, and an alternative plan which provided for an addition to be built over the auditorium up to the level of the fifth story, set back from the street, and new construction to be built on the present vacant yard, which would provide more adequate facilities for the Library, and an exterior more in keeping with the general style of the building. Estimates were obtained on these alternative projects and it was found that the smaller one would cost $350,000 and the larger $450,000.

The larger plan was reported to Mr. Harkness and the matter discussed in detail with his representative with the result that Mr. Harkness has offered an extension of time of six months, until December 31, 1931, so that the Academy may have an opportunity to secure an additional $100,000 in order that the larger extension can be constructed. On May 27, 1931 the Council voted to endeavor to secure an additional $100,000 prior to December 31, 1931.

The Council feels very much gratified that it has been possible to secure gifts and pledges during the past winter sufficient to increase the endowment fund by $400,000, and is encouraged to endeavor to raise $100,000 more in the next six months.

LIBRARY NOTES

Hours During the Summer

From June 15 until September 15 inclusive, the Library will be open on week days from 9 a.m. to 5 p.m., on Wednesdays from 9 a.m. to 10:30 p.m., and on Sundays from 10 a.m. to 5 p.m.

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Weinert, H. Menschen der Vorzeit.
Stuttgart, Enke, 1930, 139 p.

Wells, H. G.; Huxley, J. S. and Wells, G. P. The science of life.
London, Cassell, [1931], 895 p.

Werner Zoege von Manteuffel, Professor der Chirurgie in Dorpat, 1857-1926.
Stuttgart, Ausland und Heimat Verlags-aktiengesellschaft, 1931, 188 p.

Williamson, N. B. A handbook on diseases of children.
Edinburgh, Livingstone, 1931, 290 p.

Wollenweber, N. Der beamtete Arzt.
Berlin, Heymann, 1930, 252 p.

Wyatt, B. L. Chronic arthritis and rheumatoid affections.
N. Y., Wood, 1930, 166 p.

Zand, (Mme.) N. Les plexus choroïdes; anatomie, physiologie, pathologie.
Paris, Masson, 1930, 140 p.

PROCEEDINGS OF ACADEMY MEETINGS

MAY

Stated Meetings

Thursday Evening, May 7, at 8:30 o'clock

ORDER

I. Executive Session
Election of Fellows
II. Hermann Michael Biggs Memorial Lecture:
The Control of Chronic Diseases, George H. Bigelow, Commissioner of Public Health, State of Massachusetts.

Thursday Evening, May 21, at 8:30 o'clock

I. Executive Session of the Academy
Election of Fellows
II. The Eighth Harvey Lecture
"Tissue Resistance and Immunity," Frederick P. Gay, College of Physicians and Surgeons, Columbia University

Alfred E. Cohn, President Harvey Society
Dayton J. Edwards, Secretary Harvey Society

Section Meetings

Section of Surgery

Friday Evening, May 1, at 8:30 o'clock

ORDER

I. Executive Session
a. Election of Officers:
For Chairman—Robert H. Kennedy
For Secretary—William Barclay Parsons, Jr.
For member of Advisory Committee—Otto C. Pickhardt
b. Reading of the Minutes
II. Presentation of Cases
a. 1. Fracture of the head of the radius (5 cases)
2. Suppurative pericarditis—recovery by aspiration, J. V. Bohrer
b. Cases illustrating the papers of the evening, Edward C. Brenner, Nelson W. Cornell
III. Papers of the Evening
a. Total volvulus, Edward C. Brenner
b. Intestinal obstruction with a report of 230 cases, Nelson W. Cornell
IV. General Discussion

Section of Dermatology and Syphilology
Tuesday Evening, May 5, at 8:30 o'clock

ORDER

I. Executive Session
   a. Election of Officers:
      For Chairman—Joseph J. Eller
      For Secretary—Leo Spiegel
      For member of Advisory Committee—George M. MacKee
   b. Reading of the Minutes
II. Presentation of Cases
   a. Cases from Mt. Sinai Hospital
   b. Brief demonstration by Dr. Joseph H. Globus and Dr. Sol. Ginsburg on "salvarsan pericapillary encephalorrhagia"
III. General Discussion

Examination of cases is limited to members and their invited guests.

Section of Otology
Friday Evening, May 8, at 8:30 o'clock

ORDER

I. Executive Session
   a. Election of Officers:
      For Chairman—René H. Huvelle
      For Secretary—Marvin F. Jones
      For member of Advisory Committee—Hugh B. Blackwell
   b. Reading of the Minutes
II. Report of Cases
   a. Bilateral labyrinthine hemorrhage in a case of aplastic anemia, M. Rosenbluth (by invitation)
   b. Two unusual cases of labyrinthitis, Charles Manley Griffith (by invitation)
III. Paper of the Evening
   Vestibular tests on animals with experimental lesions of the nervous system, with lantern demonstration, F. H. Pike, Ph.D., Columbia University (by invitation), Page Northington (by invitation)
IV. General Discussion

Joint Meeting
of the
Section of Neurology and Psychiatry
and
The New York Neurological Society
Tuesday Evening, May 12, at 8:30 o'clock

ORDER

I. Executive Session
   a. Election of Officers:
      For Chairman—Joseph H. Globus
      For Secretary—Byron Stookey

For members of Advisory Committee—Michael Osnato, 5 years; Thomas K. Davis, 1 year (to fill the unexpired term of Byron Stookey, resigned)

b. Report of the committee appointed to outline new qualifications for Fellowship in the Academy

c. Reading of the Minutes

II. Clinical Presentations

a. Postoperative result of a chronic right sided hematoma with ipsolateral pyramidal tract signs, Ira Cohen

b. From the Neurological Institute

1. Family periodic paralysis (motion pictures), Edwin G. Zabriskie, Angus MacDonald Frantz

2. Hypertrophic interstitial neuritis, Charles A. McKendree, A. H. Rubinowitz (by invitation)

III. Papers of the Evening

a. The effects of total removal of the left temporal lobe in right handed persons; localization areas of the brain concerned with speech, Walter E. Dandy, Johns Hopkins Hospital, Baltimore (by invitation)

b. The extradural ventral chondromas. Their favorite sites, the spinal cord and root symptoms they produce and their surgical treatment, Charles A. Elsberg

IV. Discussion—Foster Kennedy, Charles A. Elsberg, Israel Strauss, Henry A. Riley, Byron Stookey, Joseph E. J. King, Leo Davidoff (by invitation)

V. General Discussion

Section of Historical and Cultural Medicine

Wednesday Evening, May 13, at 8:30 o'clock

ORDER

I. Executive Session

a. Election of Officers:

For Chairman—Karl Vogel

For Secretary—Howard Reid Craig

For member of Advisory Committee—Frederick Peterson

b. Reading of the Minutes

II. Papers of the Evening

a. A note on the medical works of Oliver Wendell Holmes, Edgar M. Bick (by invitation)

b. Rabanus Maurus, "De Rebus Divers," 1467 Incunabula Medica No. 1 (Osler), Everett Colgate Jessup

c. Early literature on arthritis, with exhibits, Reginald Burbank

III. General Discussion

Section of Pediatrics

Thursday Evening, May 14, at 8:30 o'clock

ORDER

I. Executive Session

a. Election of Officers:

For Chairman—Herbert B. Wilcox
For Secretary—John Caffey
For member of Advisory Committee—Hugh Chaplin

b. Reading of the Minutes

II. PAPERS OF THE EVENING

a. A method for the continuous infusion in infants, John Mitchell Brush (by invitation)

b. The treatment of toxicosis with the aid of a continuous intravenous drip of glucose solution, Samuel Karelitz
Discussion, Bela Schick

c. A comparison of the blood chemistry in intestinal intoxication of infants, and in adrenalectomized animals. Treatment of intestinal intoxication with an adrenal cortex extract, Aubrey B. MacLean, Ruth Sullivan (by invitation), R. L. Zwemer (by invitation)

III. GENERAL DISCUSSION

SECTION OF ORTHOPEDIC SURGERY

ORDER

I. EXECUTIVE SESSION

a. Election of Officers:
For Chairman—Isadore Zadek
For Secretary—Mather Cleveland
For member of the Advisory Committee—Alan DeForest Smith

b. Reading of the Minutes

II. PRESENTATION OF CASES

a. The result of reconstruction of flexor tendon in a finger by fascial graft, Mather Cleveland

b. Cases illustrating the treatment of tennis elbow, Louis Carp

III. PAPERS OF THE EVENING

a. Tennis elbow as caused by radiohumeral bursitis. Its anatomical, clinical, roentgenological and pathological aspects, with a suggestion as to treatment, Louis Carp

b. 1. Tensile strength and elasticity tests of human fascia lata
2. A new needle and suture carrier for living sutures, Charles Murray Gratz (by invitation)

IV. GENERAL DISCUSSION

SECTION OF OPHTHALMOLOGY

Monday Evening, May 18, at 8:30 o'clock

ORDER

I. EXECUTIVE SESSION

a. Reading of the Minutes

b. Election of Officers:
For Chairman—Mark J. Schoenberg
For Secretary—Algernon B. Reese

For members of the Advisory Committee—Ernest F. Krug, 5 years; Bernard Samuels, 3 years (to fill unexpired term of Edgar S. Thomson, deceased)

II. Case Presentation

a. 1. A modified Motais operation

2. Two cases of exenteration with skin graft (lantern slides), Daniel B. Kirby

b. Total ophthalmoplegia, Joseph S. Hory

III. Demonstrations

a. Cysts of the cornea (lantern slides), Milton L. Berliner

b. 1. Hemorrhage within optic nerve sheath in an irradiated fetus (lantern slides)

2. Spongio-neuroblastoma of optic nerve, in von Recklinghausen disease (lantern slides), David Wexler, Isadore Goldstein

IV. Paper of the Evening

Syphilitic optic atrophies, Joseph Earle Moore, Baltimore (by invitation)

V. General Discussion

Section of Medicine

Tuesday Evening, May 19, at 8:30 o'clock

ORDER

I. Executive Session

a. Election of Officers:

For Chairman—Harold E. B. Pardee

For Secretary—Robert F. Loeb

For member of Advisory Committee—Lewis F. Frissell

b. Reading of the Minutes

II. Papers of the Evening

a. Recent important contributions to nephritis, Arthur M. Fishberg

Discussion, Herman O. Mosenthal, George Baehr

b. Recent contributions in tuberculosis treatment, Edgar Mayer, Saranac Lake (by invitation)

Discussion, S. Adolphus Knopf, Henry T. Chickering, Marion B. Sulzberger

c. Recent progress in diseases of metabolism, Walter W. Palmer

Discussion, Eugene F. DuBois

III. Informal Discussion

Section of Genito-Urinary Surgery

There was no meeting of the Section in May.

Section officers for the ensuing year were elected at the April meeting as follows:

Chairman—Meredith F. Campbell

Secretary—George F. Hoch

Member of Advisory Committee—Archie L. Dean, Jr.

Section of Obstetrics and Gynecology

Tuesday Evening, May 26, at 8:30 o'clock

ORDER

I. Executive Session
   a. Election of Officers:
      For Chairman—Gerard L. Moench
      For Secretary—Francis W. Sovak
      For member of Advisory Committee—Hervey C. Williamson
   b. Reading of the Minutes
II. Case Reports and Presentation of New Instruments
   a. Pelvic insufflation syringe, Francis W. Sovak
   b. An unusual case of neonatal pulmonary atelectasis, Joseph E. Corr (by invitation)
III. Papers of the Evening
   a. Postural treatment of intracranial hemorrhage in the new-born, Edwin A. Riesenfeld
      Discussion opened by Leo Davidoff (by invitation), Morris Leff, Simon Robert Thau
   b. The development of the inner female sexual organs, Prof. Ete Burg, Pecs University, Hungary (by invitation)
      Demonstration by models
IV. General Discussion
V. Discussion of qualifications for Fellowship in the Section following the report of the Special Committee

Section of Laryngology and Rhinology

Wednesday Evening, May 27, at 8:30 o'clock
at the
Academy of Medicine

ORDER

I. Executive Session
   a. Election of Officers:
      For Chairman—Westley M. Hunt
      For Secretary—Arthur S. Wilson
      For member of Advisory Committee—Duncan Macpherson
   b. Report of Advisory Committee on qualifications for Fellowship in Rhino-Laryngology
   c. Reading of the Minutes
II. Report of Cases:
   Foreign body in lung—2 cases, George R. Brighton
III. Papers of the Evening
   a. Studies in sinus infection, J. Wynne Pugh (by invitation)
   b. Paralysis of the vocal cords, Alfred Michaelis
   c. Agranulocytic angina, James W. Babcock
IV. General Discussion

THE NEW YORK ROENTGEN SOCIETY
In Affiliation with
THE NEW YORK ACADEMY OF MEDICINE
Monday Evening, May 18

ORDER

I. 8:30 P. M.
Demonstration of interesting cases and roentgenograms
II. 9:00 P. M.
a. Observations on the application of large doses of highly filtered high potential x-rays, Maurice Lenz
b. Comparison of filters in high voltage roentgen therapy, Mr. C. B. Braestrup (by invitation)
c. The changes in quality of roentgen rays after their passage through tissue, Edith Quimby, Robert McNattin
III. GENERAL DISCUSSION
To be opened by Francis Carter Wood, G. Failla
IV. EXECUTIVE SESSION
ROSS GOLDEN, President
J. BENNETT EDWARDS, Secretary

NEW YORK MEETING
of the
SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE
Under the auspices of
THE NEW YORK ACADEMY OF MEDICINE
Fifth Avenue and 103 Street
Wednesday, May 20, 1931, at 8:15 P. M.

I. Regeneration of Virus Myxomatosum (Sanarelli) in the Presence of Cells of Exudates Surviving *in Vitro*, B. Benjamin and T. M. Rivers
II. Streptococcus Leucocidin and Clasmatocyte Resistance, F. P. Gay and F. Oram
III. Oral Immunization of Humans Against Pneumococcus as Determined by Increased Protective Antibody Content of Serum, V. Ross
IV. Spermagglutination by Bacteria, L. Rosenthal
V. Biochemical Studies of Human Semen. Factors Affecting Migration of Sperm Through the Cervix, E. G. Miller, Jr., and R. Kurzrok
VI. Rate of Decalcification and the Sites of Bone Lesions in Experimental Hyperparathyroidism, H. L. Jaffe, A. Bodansky and J. E. Blair
VII. A Study of the Allergic Phenomena in the Central Nervous System, C. G. Burn and K. H. Finley (introduced by R. Hussey)
VIII. The Permeability of the Lymphatic Wall, P. D. McMaster and S. S. Hudack

IX. The Breakdown of the Lymph Transport, S. S. Hudack and P. D. McMaster

PEYTON ROUS, President
A. J. GOLDFORB, Secretary

NEW YORK PATHOLOGICAL SOCIETY
In Affiliation with
THE NEW YORK ACADEMY OF MEDICINE
Thursday Evening, May 28, at 8:30 o'clock

ORDER

I. PAPERS OF THE EVENING
   a. A case of foreign body in the orbit, Reuben Goodman (by invitation)
   b. Osteogenic sarcoma-like tumor of the metacarpal bone, Henry L. Jaffe (by invitation), Leo Mayer
   c. Heredity of the agglutinogens M and N of Landsteiner and Levine with particular reference to determination of paternity, Alexander S. Wiener (by invitation), Max Lederer
   d. Brain lesions in influenza, Irving Sands (by invitation)
II. EXECUTIVE SESSION

LEILA CHARLTON KNOX, President, St. Luke's Hospital
BERYL H. PAIGE, Secretary, The Babies' Hospital

DR. PAOLO DE VECCHI

Dr. Paolo De Vecchi of New York and formerly of San Francisco, was born in Quattordio, near Turin, Italy, on September 26, 1847. His parents were Margherita Berruti and Dr. Guiseppe De Vecchi, the latter an eminent physician of Turin. He died May 30, 1931.

In 1872, he received his medical degree from the University of Turin. Soon after graduating, he was made Assistant Surgeon of St. John's Hospital of Turin and was later appointed Court physician to H. R. H. the Prince Amedeo of the House of Savoy.

While a student at the University, he volunteered with General Guiseppe Garibaldi and served in the Roman campaign of 1867 and was severely wounded at the battle of Monterotondo (near Rome).

Three years later, in 1870, he volunteered in the Franco-Prussian War as surgeon with the "Ambulance Turinoise" of the Red Cross which was in action at the battle of Sedan. For his services he received decorations from the French and Italian Governments.

In 1873, he was sent by the Italian Government to South America for scientific study and to make a thorough survey of Italian emigration in South America. He received a decoration from his Government for the work accomplished. In 1880, obtained a five months' leave of absence from Prince Amedeo of Savoy and St. John's Hospital, for the purpose of visiting the United States where he was desirous of studying orthopedic surgery under the well known surgeon, Professor Louis Sayre of New York, and other surgeons of Boston and Baltimore, and also to visit and study American hospitals and methods.

While in New York, he was invited to perform an operation in San Francisco, where he finally settled and practised surgery for twenty-five years. He introduced on the Pacific Coast the Lister method of antisepsis.

In 1885, he married Miss Margaret Follis of San Francisco and they had three children. He became a naturalized citizen of the United States in 1887. During his residence in California, he acted as correspondent for two important daily newspapers and several medical journals in Italy. He also edited in San Francisco, "The Lancet," a medical journal, and contributed a great many articles on medicine and surgery to medical journals here and abroad. His most recent and important publications are:

"Modern Italian Surgery"

"A Discourse on Divorce"

"How Italy Won the War" (translation of a book written by Colonel Edgar E. Hume of the U. S. Army Medical Corps).

In 1905, he retired after a most successful and brilliant medical career and devoted his time to travel and writing. In 1910 he settled in New York and established a residence at 43 Fifth Avenue.

He received from His Majesty the King of Italy, for services rendered, the decoration of:

Cavaliere della Corona d'Italia—and also

Commendatore dei S. S. Maurisio e Lazzaro—
one of the highest decorations awarded to civilians by the Italian Government. He was also awarded a number of other decorations for his military, scientific and philanthropic works.

In California, he was actively identified in business and charitable works besides his medical profession. He organized a number of charities for his countrymen living in California and he was the founder of St. Joseph's Hospital, which is now the largest public hospital in San Francisco, and also the Adler Hospital, now known as the Dante Sanitorium, in San Francisco. He was one of the organizers, and for a time was President of the Italian Swiss Colony, a very large agricultural colony in the northern part of Cali-

fornia, as also the Italian-American Bank which was lately absorbed by the Bank of America of California. In New York, he served as a trustee of the Mulberry Community House and the Italian Welfare League and as a Director of the Banca Commerciale Italiana and as a Director of the Di Giorgio Fruit Corporation.

Dr. De Vecchi was elected a Fellow of the Academy January 3, 1918; he was a member of the Royal Academy of Turin, Fellow of the American College of Surgeons, Member of Medical Society of the State of New York and State of California, a member of the University Club of New York, life member of the Dante Alighiere, life member of The California Academy of Science, founder and charter member of the Olympic Club of San Francisco, one of the founders of the Burlingame Country Club, The Family Club, the Sierra Club of San Francisco and a member of the Bohemian and Pacific Union Clubs of San Francisco and a member of the Geographic Society of California.

DEATHS OF FELLOWS OF THE ACADEMY

JOSEPH BERNARD COHEN, M.D., 948 Grand Concourse, New York City; graduated in medicine from New York University and Bellevue Hospital Medical College, New York City, in 1907; elected a Fellow of the Academy November 6, 1919; died, May 29, 1931. Dr. Cohen was a Fellow of the American Medical Association, a member of the County and State Medical Societies, a member of the Society of Alumni of Lebanon Hospital and Associate Physician to Lebanon Hospital.

CHARLES NORTH DOWD, M.D., 149 Lake Avenue, Saratoga Springs, N. Y.; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1886; elected a Fellow of the Academy December 5, 1889; died, May 24, 1931. Dr. Dowd was a Fellow of the American Medical Association, a Fellow of the American College of Surgeons; a member of the County and State Medical Societies, a member of the American Surgical Association, a member of the International Surgical Society and a member of the New York Surgical Society; a member of the Roosevelt Hospital Alumni Association, Consulting Surgeon to Roosevelt, Memorial, St. Mary's Hospital for Children and Saratoga and Reconstruction Unit of Post-Graduate Hospital. While in New York Dr. Dowd was Professor of Clinical Surgery at the College of Physicians and Surgeons.